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THE LANCET

No. 7037 LONDON SATURDAY 12 JULY 1958 VOL. II FOR 1958

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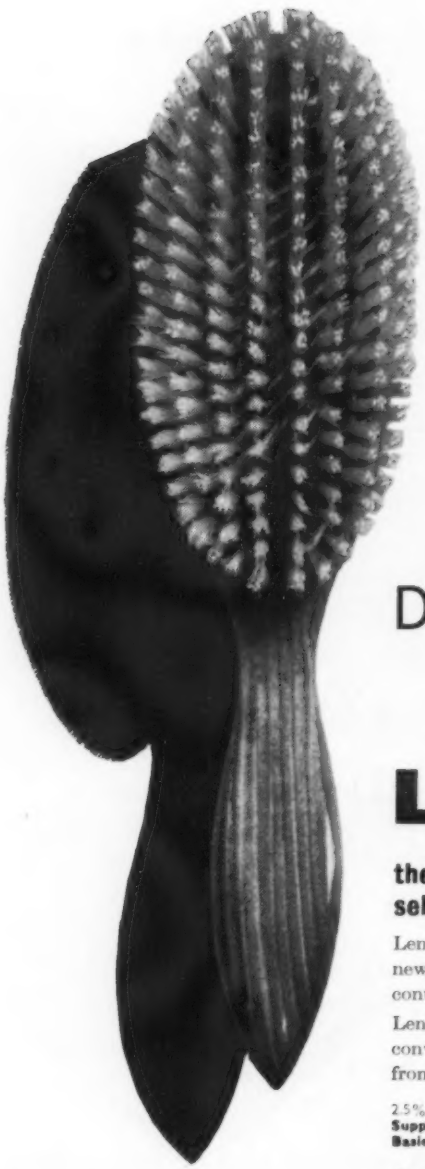

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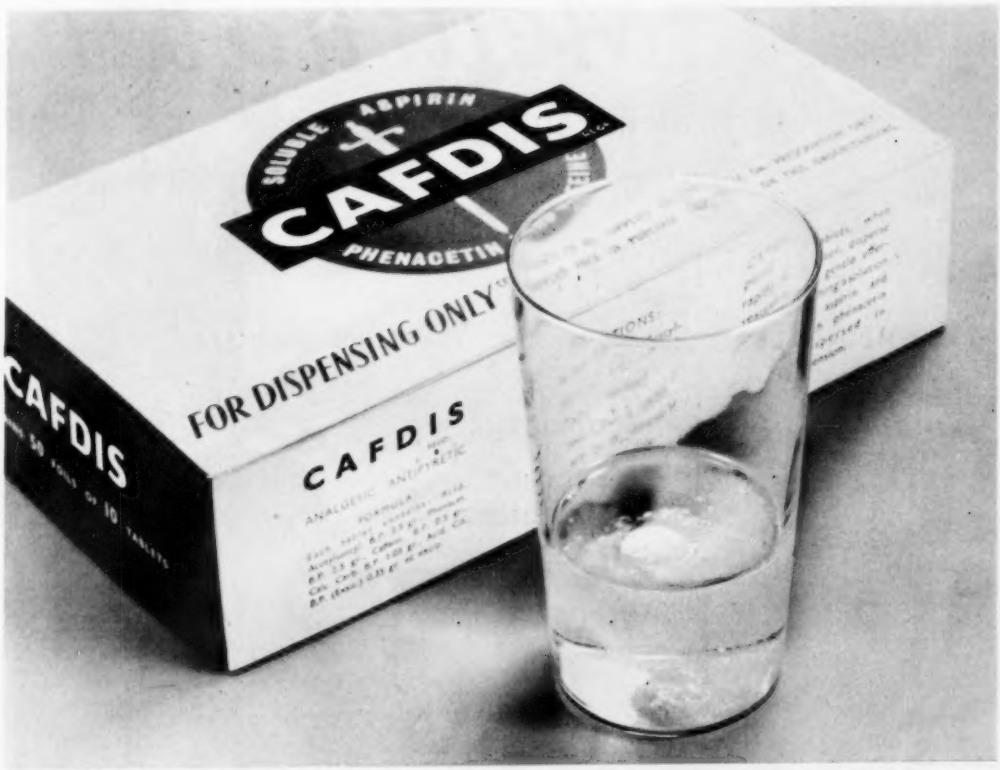

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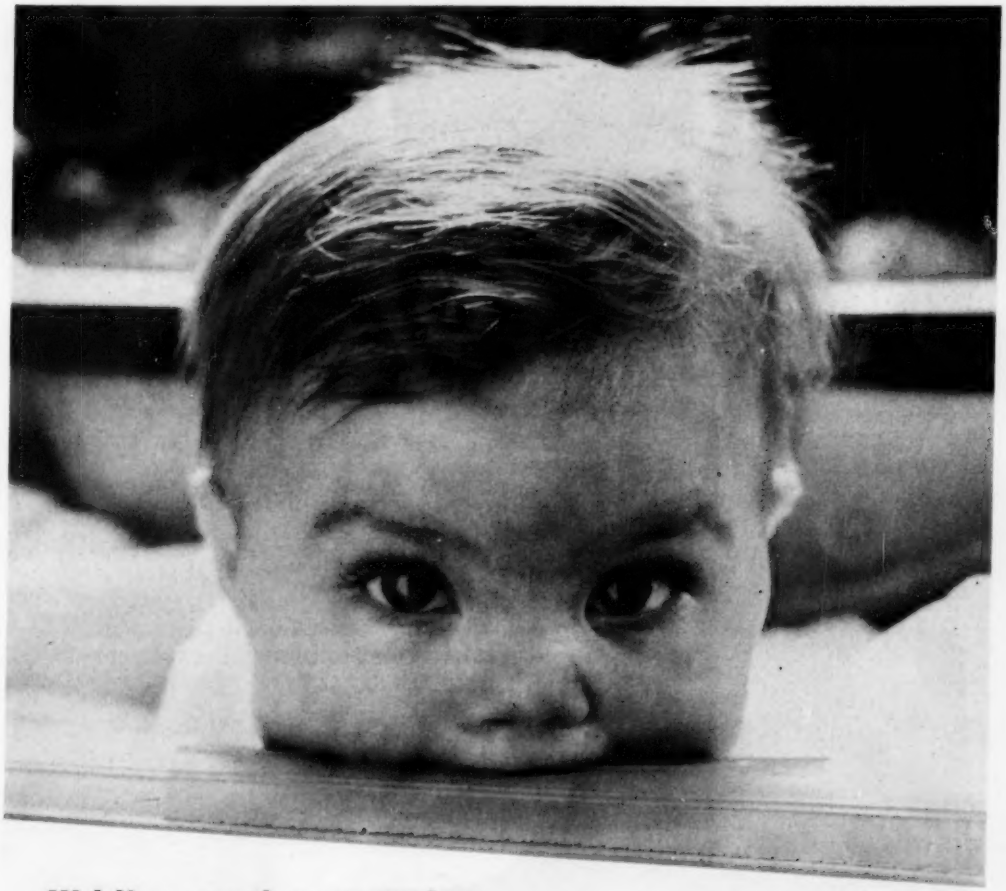

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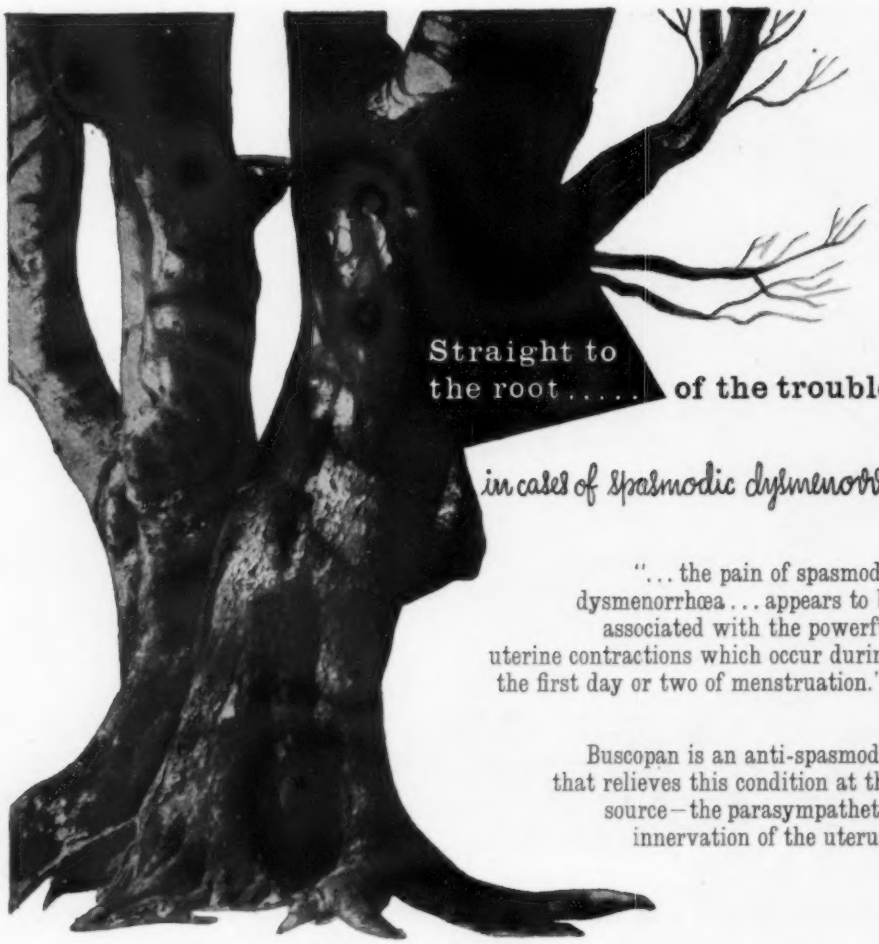

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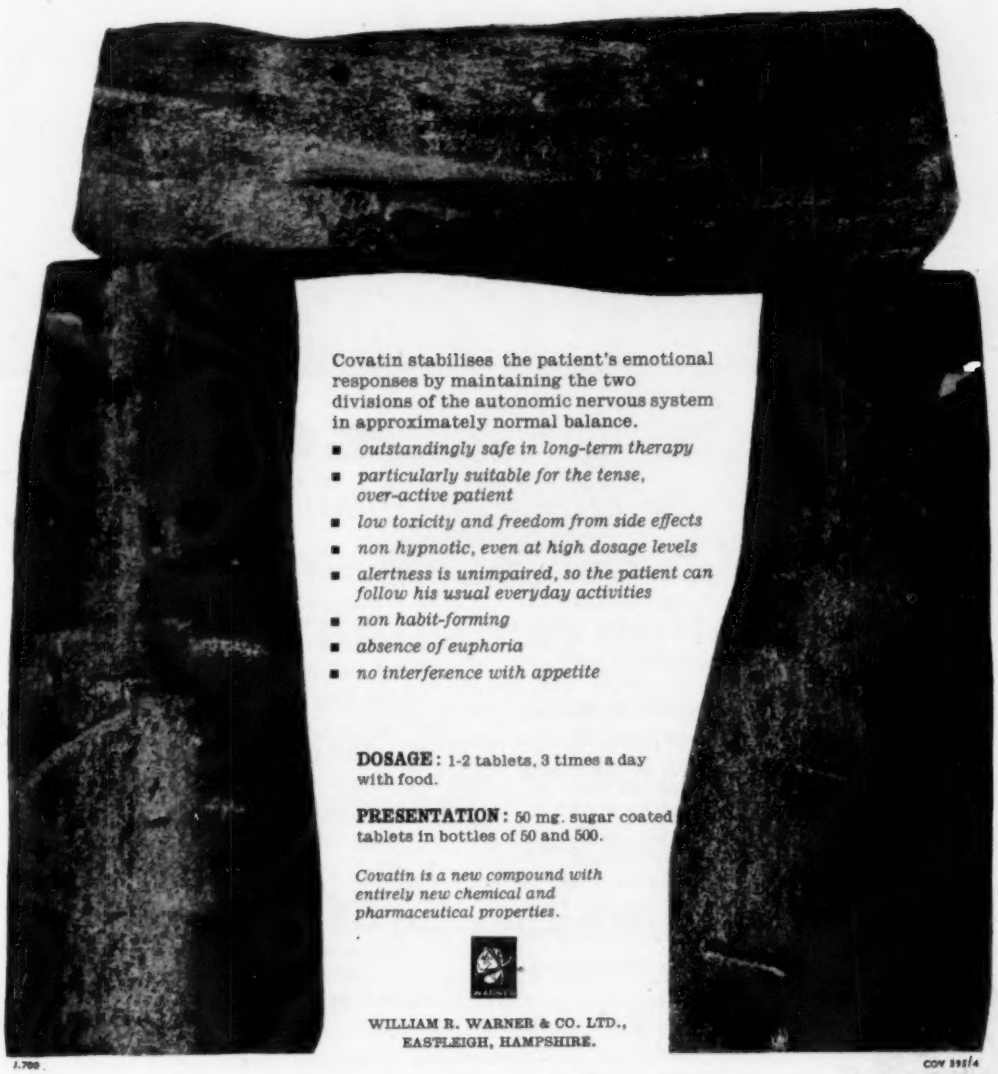

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1. *Nature*, 1955, *175*, 388.
2. *B.M.J.*, 1956, *1*, 142.
3. *B.M.J.*, 1955, *1*, 1367.
4. Annotation (1956), *B.M.J.*, *1*, 161.
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6. *Practitioner*, 1957, *179*, 1071.

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Therapeutische Umschau 1952, 8, 143.

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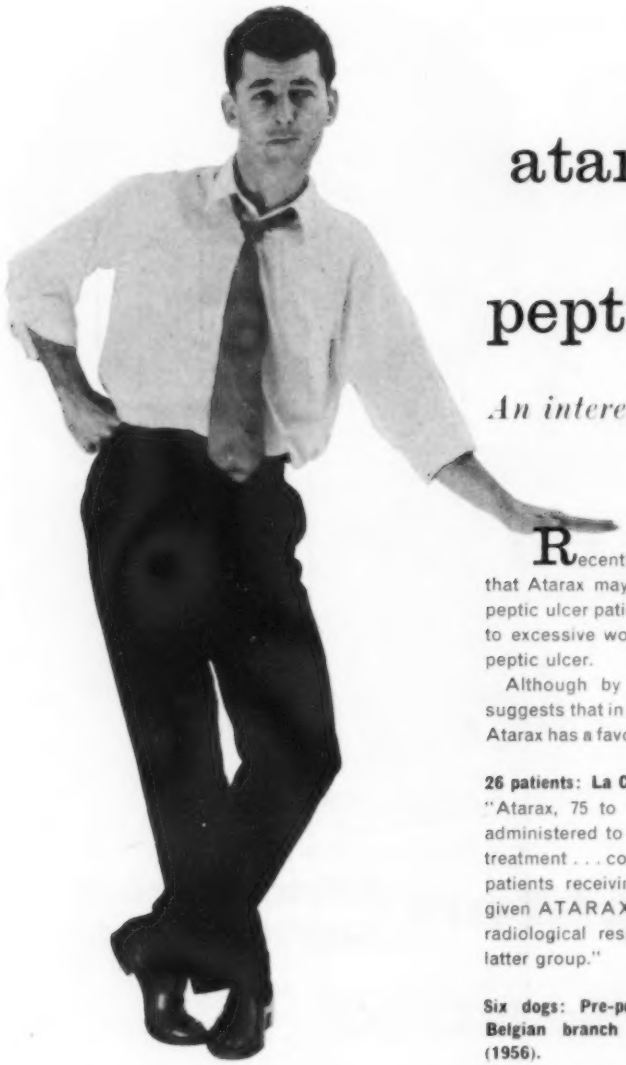

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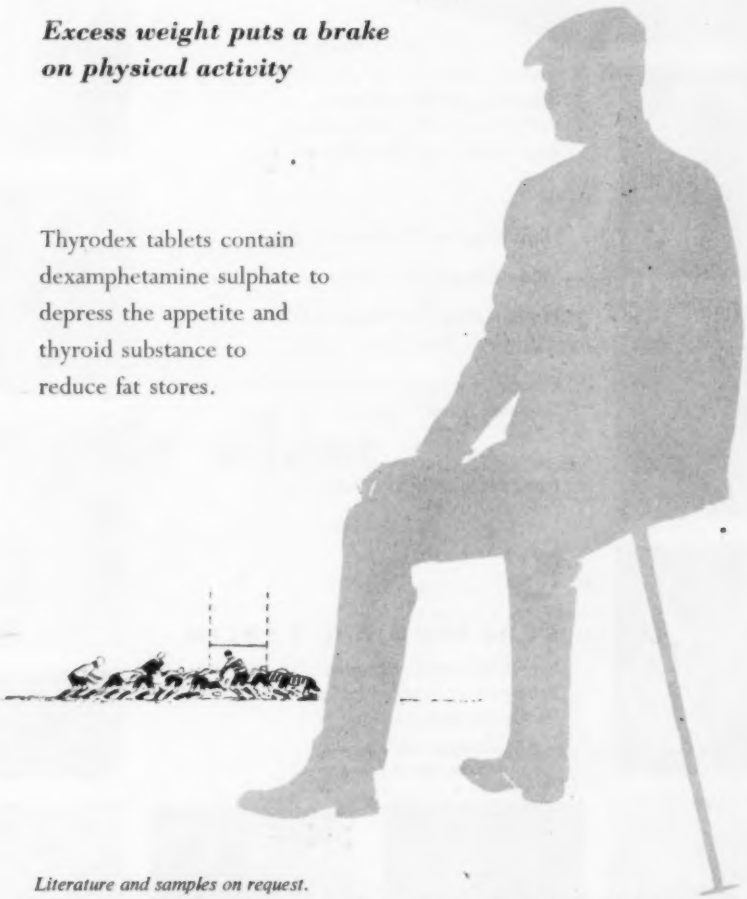

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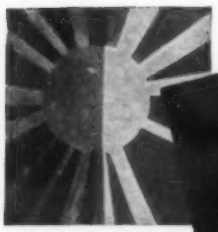

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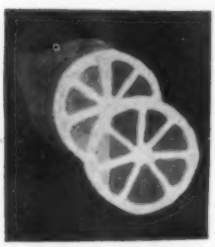

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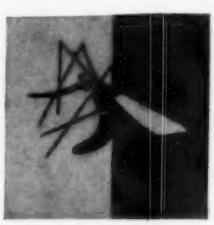

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*Reference: Nature, May 17th, 1958, p.1397

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*"The Oral Treatment of Pernicious Anaemia: A New Approach." Lancet (1958), 1, 982.

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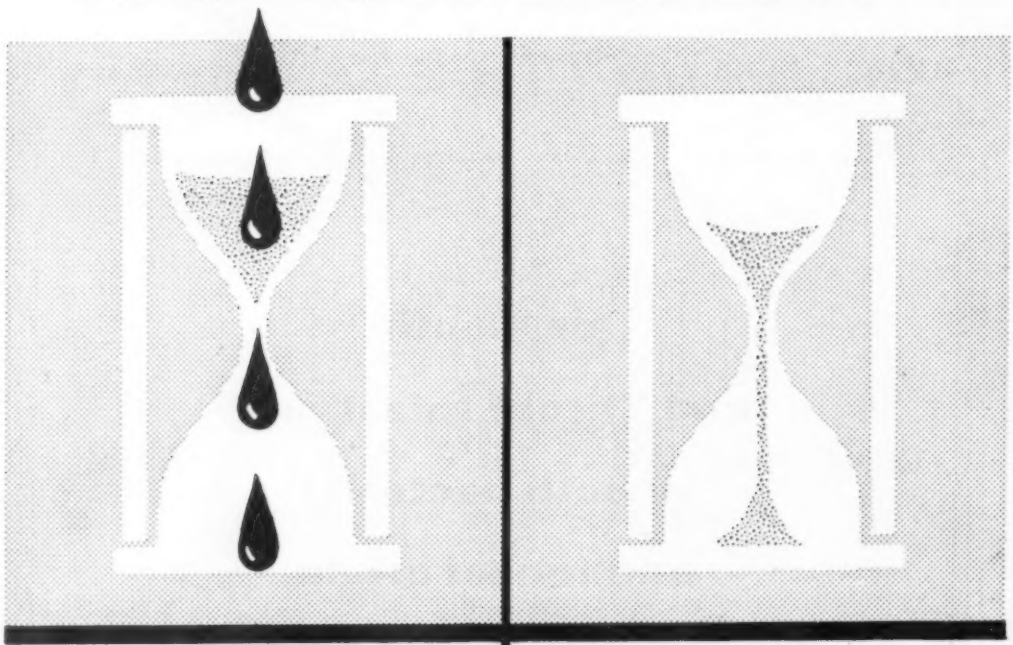

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References

Anaesthesia, adrenoxyl ad perfusionem and the reduction of blood loss. *Anaesthesia*, 1958, **13**, 56
(*The adrenoxyl ad perfusionem was specially prepared in a strength and solution suitable for administration by intravenous drip.*)
Anaesthesia for Fractures of the Femoral neck. *Lancet* 1957, **1**, 1092
Principles of Surgical Technique. *Brit. Med. J.*, 1956, **1**, 925

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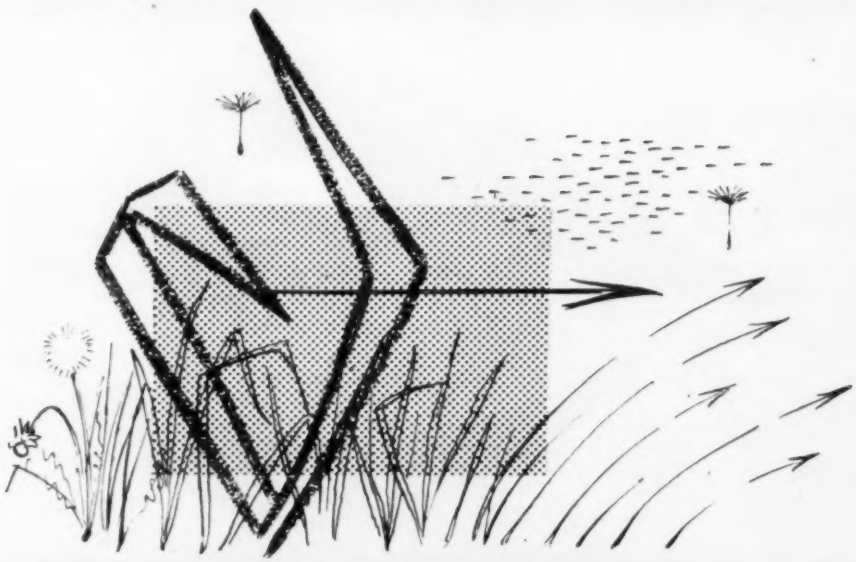

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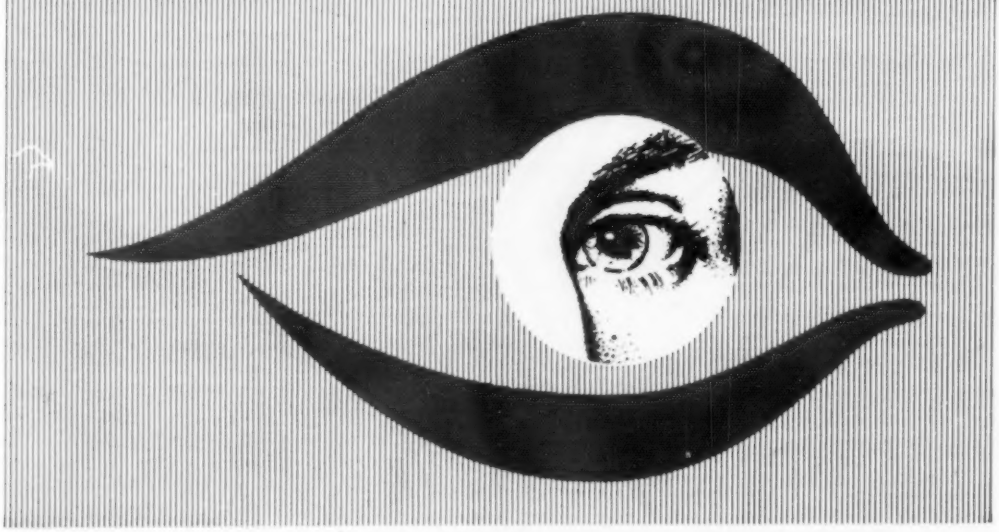

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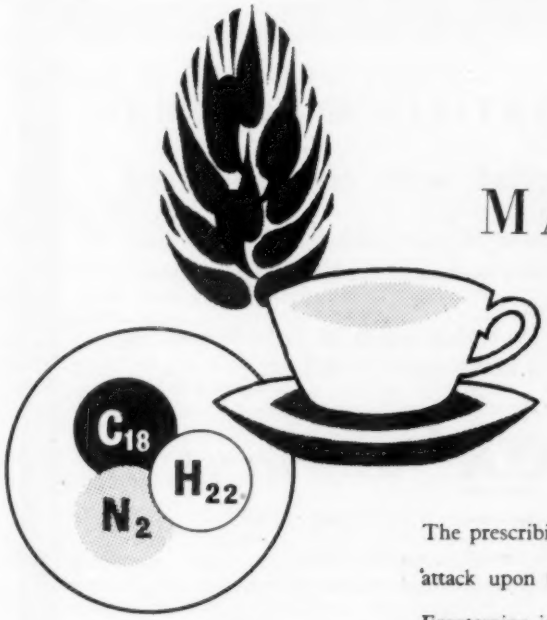

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THE ROLE OF ENDOGENOUS PYROGEN IN THE GENESIS OF FEVER *

W. BARRY WOOD, JR.
M.D. Johns Hopkins
PROFESSOR OF MICROBIOLOGY
From the Department of Microbiology, Johns Hopkins University School of Medicine and School of Hygiene and Public Health, Baltimore, Maryland

THE view that fever and inflammation are intimately related is more than a hundred years old. In 1851 Zimmermann [48] suggested that fever might be caused by products of inflammatory lesions. His suggestion received prompt support from a number of investigators, who succeeded in preparing from purulent exudates a variety of extracts which, when injected intravenously, produced fever.[13 19 24 45] In the light of subsequent evidence it is significant that at least some of these early preparations were relatively resistant to heat.

Pyrexin

In 1943 Menkin [32] separated from inflammatory exudates a pyrogenic euglobulin fraction which he later named "pyrexin". It too was heat-stable; even when boiled, it retained its full activity.[33] In this regard it resembled bacterial pyrogens.[8] More recent studies have revealed that pyrexin has many of the other properties of pyrogenic bacterial endotoxins.[10] Like them, it produces fever only after a relatively long latent period when injected intravenously; it causes an appreciable leucopenia after the injection; it induces a state of refractoriness, known as tolerance, when administered repeatedly†; and its pyrogenic effect is much depressed when it is injected into animals previously made tolerant to other bacterial pyrogens. Indeed its resemblance to bacterial pyrogens is so striking that Menkin [34] concludes that pyrexin may be a "complex" of bacterial pyrogen with serum-globulin.

* The studies from the author's laboratory which are referred to in this article were supported by a grant from the Life Insurance Medical Research Fund. They were made in collaboration with Elisha Atkins, M.D., of the department of medicine, Yale University School of Medicine, New Haven, Connecticut; and M. Kenton King, M.D., of the departments of medicine and preventive medicine, Washington University School of Medicine, St. Louis, Missouri.

† Menkin's (1955) finding that pyrexin, when given in large enough doses, does not produce tolerance, does not invalidate the earlier observation [10] that it does so when given in smaller doses. It has been clearly established that tolerance to bacterial pyrogens may be wholly masked, if the doses used in the repeated injections are sufficiently large.[28]

Leucocytic Pyrogen

Five years after Menkin's report, a fever-producing substance with very different properties was extracted from polymorphonuclear leucocytes by Beeson.[3] Unlike pyrexin and bacterial pyrogens, the leucocytic pyrogen was eventually found to have the following properties: (1) it was relatively heat-labile [10]; (2) it caused a briefer febrile response (after a relatively short latent period) [10]; (3) it caused little, if any, post-injection leucopenia [10]; (4) it was fully active in recipients tolerant to bacterial pyrogens [8]; (5) it did not produce tolerance when repeatedly injected [10]; and (6) it was, at least to some extent, species-specific in its action.[36]

This last property is of particular interest in relation to Menkin's original experiments. Whereas he demonstrated that pyrexin extracted from inflammatory exudates in dogs was pyrogenic to rabbits, Petersdorf and Bennett [36] find that the pyrogen contained in canine leucocytes is inactive in rabbits. Clearly, leucocytic pyrogen and pyrexin are two different substances.

The accompanying table shows that each of the characteristic properties of pyrexin is common not only to bacterial pyrogens but also to the toxic polysaccharides extracted chemically from normal tissues by Landy and Shear.[30] In contrast, none of these properties is shared by leucocytic pyrogen.

Transferable Pyrogen

In 1953 Grant and Whalen,[21] studying the pyrexial response of rabbits to typhoid vaccine, detected in their sera, as long as three hours after the injection of the vaccine, a component which produced fever when injected intravenously into a second set of rabbits. Having shown that typhoid vaccine previously incubated with normal rabbit plasma caused the same kind of prompt response as that induced by the transferable pyrogen, they concluded that the latter was formed by an interaction of the originally injected bacterial endotoxin with the plasma.

Two years later Atkins and Wood [1 2] showed that the transferable pyrogen detected by Grant and Whalen [21] was quite separate from bacterial endotoxin. Whereas the endotoxin was rapidly cleared from the blood-stream, the transferable pyrogen persisted throughout the febrile response, and its concentration in the circulation was directly proportional to the intensity of the fever.[2] The newly discovered factor appeared to be endogenous and was biologically indistinguishable from leucocytic pyrogen (see table).

COMPARATIVE PROPERTIES OF PYROGENS

Pyrogen	Stability to heat *	Relative length of latent period	Post-injection leucopenia	Activity when injected into tolerant recipients	Production of tolerance	Action on thermoregulatory centres when in circulation
Bacterial endotoxins [8]	Stable [8]	Long [8]	Marked [8]	Depressed [8]	Yes [8]	Indirect [37] †
Pyrexin [33]	Stable [33]	Long [10]	Marked [10]	Depressed [10]	Yes [10]	§
Chemically extracted tissue polysaccharides [30]	Stable [30]	Long [30]	Marked [30]	Depressed [30]	Yes [30]	§
Leucocytic pyrogen [3]	Unstable [10]	Short [10]	Slight or none [10]	Unaffected [10]	No [10]	Direct [37]
Pyrogen in circulation during endotoxin-induced pyrexia [1]	? ‡	Short [2]	Slight or none [2]	Unaffected [2]	No [21]	Direct [37]
Pyrogen in circulation during febrile phase of acute bacterial infections [29]	? ‡	Short [29]	§	Unaffected [29]	§	Direct [29]

* Exposure to 90°C for 30 minutes.
† Action may be "direct" when endotoxin is in spinal fluid.[35]
‡ No satisfactory method has been developed for testing heat-stability of pyrogen in presence of serum.[35]
§ Not yet tested.

Cell-injury Hypothesis

These findings, taken in conjunction with the fact that bacterial endotoxins have both an affinity [15] and a toxicity [14 29] for leucocytes, led to the suggestion that endotoxin-induced fever is due to the activation of thermoregulatory centres of the brain by circulating endogenous pyrogen released from leucocytes injured by the endotoxin.[2] The relatively long latent period and the post-injection leucopenia, which are regularly observed in endotoxin fever,[5] appear to be in keeping with this hypothesis. Recently, Bennett, Petersdorf, and Keene [12] have reported that the formation of circulating endogenous pyrogen, which follows the intravenous injection of endotoxin, is greatly depressed in animals previously made leucopenic with nitrogen mustard. This finding also supports the suggestion that the endogenous pyrogen is of leucocytic origin.

Possible Direct Action of Endotoxin

Certain other facts relating to endotoxin-induced fever, however, have led Bennett and his co-workers [5 12 38] to question the validity of this " cell-injury theory ". They have justifiably emphasised that a fever-producing factor indistinguishable from leucocytic pyrogen is present in virtually agranulocytic exudates obtained from rabbits made leucopenic with nitrogen mustard.[10] They have also shown that such leucopenic rabbits exhibit the usual febrile response to intravenously injected endotoxins,[11] even though circulating endogenous pyrogen is not detected in their blood-streams.[12 37] Furthermore they have shown by ingenious experiments that endotoxin injected intrathecally in minute amounts promptly causes pyrexia [25]; that it does not cause tolerance if given repeatedly by this route [25]; and that, if given intravenously in sufficiently large amounts, it will " spill over " into the spinal fluid.[12] Having thus apparently dissociated the febrile response from the presence of circulating endogenous pyrogen, and having demonstrated that endotoxin in the spinal fluid is highly pyrogenic, they have postulated that the endotoxin itself may play a direct role in causing the fever.[12 38]

As mentioned elsewhere,[27 28] these observations relating specifically to endotoxin fever must be interpreted with caution. The evidence that endotoxin when introduced into the subarachnoid space will cause fever, apparently by acting on the central nervous system, is certainly conclusive. That intrathecal endotoxin should have this effect is not surprising in view of the well-known sensitivity of the thermoregulatory centres to noxious stimuli.[41] However, it should be emphasised that, after the intravenous injection of endotoxin, an apparent dissociation of the fever and the presence of circulating endogenous pyrogen has been achieved only by injecting relatively large doses of endotoxin under conditions in which the production of endogenous pyrogen is known to be depressed—i.e., in the presence of either tolerance or profound leucopenia.[12 38] Furthermore, the failure to demonstrate circulating endogenous pyrogen by the passive transfer technique [1] does not necessarily indicate that it is absent; for the test, as usually applied, is capable of detecting only relatively large amounts of the endogenous factor.[28] Sufficient endogenous pyrogen, for example, may be present in the blood of the endotoxin-injected (donor) animal to cause it to have fever, even though the amount transferred to a second (recipient) animal is insufficient to produce a febrile response. Although in special circumstances intravenously injected endotoxin, given in sufficient amount, may reach the spinal fluid and thus initiate pyrexia,[12 38] the data so far obtained do not negate the original observation that in normal animals capable of producing full amounts of endogenous pyrogen, the fever induced by moderate intravenous doses of endotoxin is directly related to the concentration of endogenous pyrogen in the blood-stream.[2]

Pyrogenic Tissue Polysaccharides

The isolation of pyrogenic polysaccharides from various normal tissues by Landy and Shear [30] raises the additional question whether these substances may not somehow be involved in the production of fever. At present it can only be stated that, since the biological properties of bacterial pyrogens and of the tissue polysaccharides have been shown to be the same [30] (see table), all the arguments against the direct action of the former pertain also to the latter. If for no other reason than that they cause tolerance, it seems unlikely that the tissue polysaccharides, at least in the form isolated by Landy and Shear,[30] are directly responsible for natural pyrexia. Were the causal pyrogen in the circulation capable of producing tolerance, pyrexia due to systemic disease could not be expected to be fully sustained for more than a few days. It is conceivable, however, that tissue polysaccharides may eventually be shown to be released during cellular injury and, when so released, to cause the production of endogenous pyrogen. There is as yet no evidence either for or against this interesting possibility.

Source and Site of Action of Endogenous Pyrogen

While the above-mentioned investigations of Bennett et al. were in progress, further studies were undertaken relating to the source and the site of action of endogenous pyrogen. Polymorphonuclear leucocytes were found to be the principal source of endogenous pyrogen in granulocytic exudates and were observed to discharge their pyrogenic component into the surrounding medium while still motile and apparently otherwise functionally intact.[26] Both the endogenous pyrogen derived from leucocytic exudates and that present in the serum during endotoxin-induced fever were also found to exert their pyrogenic effects, when introduced into the circulation, by acting directly on the thermoregulatory centres of the brain.[27] Circulating bacterial (exogenous) pyrogen, on the other hand, was shown to act by a different and less direct mechanism.[27]

" Natural Fever " Models

Because both endogenous and exogenous pyrogens may, in certain circumstances, act on the cerebral centres to cause endotoxin-induced fever, this widely used experimental model is not entirely satisfactory for studying the pathogenesis of fever in general.[27] Not only is it a relatively artificial model involving the injection of toxic foreign substances, but also it is characterised by certain features which appear to have no counterpart in naturally occurring pyrexia—e.g., tolerance.[5] Hence, studies must be extended to other experimental models, designed to simulate more closely the conditions of naturally occurring pyrexia. Two such models have recently been investigated.

In 1956 Bennett [7] reported extensive investigation of the fever of experimental pneumococcal peritonitis in rabbits. During the febrile phase of the infection he found, in both the peritoneal exudate and the thoracic-duct lymph, a heat-labile substance which appeared to be identical with leucocytic pyrogen. Its presence at both

sites correlated closely with the animal's fever. When defervescence was produced by penicillin therapy, the pyrogen was no longer detected in the exudate. Although, in the latter circumstances, leucocytes were still plentiful in the peritoneal exudate, control of the infection apparently removed the stimulus which previously had caused the production of endogenous pyrogen. The ability of the blood-stream to rid itself promptly of intravenously injected leucocytic pyrogen had already been established in an earlier study.[6] Despite these important and highly suggestive findings, Bennett was unable to demonstrate the fever-producing factor in the blood-stream during the active infection. Accordingly he was forced to conclude that the possible causal relationship between the fever and the endogenous pyrogen in the exudate and lymph had not been established.

The demonstration of circulating pyrogen in such an experimental model is obviously crucial.[6 39 42 46 47] A concerted attempt was therefore made to detect its presence at the height of the febrile phase of the infection. When a passive-transfer method was used, in which considerably larger volumes of serum were employed than had been tested by Bennett, a pyrogen similar to that noted in the pneumococcal exudate and lymph was found to be present in the blood-stream.[28] The transferable factor in the circulation was also shown to act directly on the thermoregulatory centres.[28] Since the endogenous pyrogen in acute granulocytic exudates has been shown to come from polymorphonuclear leucocytes,[26] it now appears to be established beyond reasonable doubt that the fever of pneumococcal peritonitis in rabbits is caused by a circulating endogenous pyrogen produced by the polymorphonuclear leucocytes in the peritoneal exudate and carried to the blood-stream via lymphatic channels emptying into the thoracic duct.[28]

Similar results were obtained with a second experimental model—i.e., one involving acute streptococcal cellulitis. During the febrile phase of this infection also, an apparently identical endogenous pyrogen has been demonstrated in the blood-stream.[28]

In spite of the evidence provided by these latest experiments, the question may still be raised whether bacterial pyrogens do not play at least a secondary role in the production of pyrexia caused by experimental infections. In pneumococcal peritonitis this possibility seems highly unlikely for the following reasons:

(1) No bacterial pyrogen has ever been detected in pneumococcal cultures.[7]

(2) The pyrogen detected by Bennett in the peritoneal exudate and thoracic-duct lymph was completely inactivated by being heated at 90°C for 30 minutes, did not produce tolerance when repeatedly injected, and was equally active in tolerant and normal recipients.[7] In short, no heat-stable component compatible with a bacterial pyrogen was detected in either the exudate or the lymph.

(3) The factor found in the blood-stream was unlike bacterial pyrogen in that (*a*) its activity was the same in normal and tolerant recipients, and (*b*) its pyrogenicity was due to a direct effect on the thermoregulatory centres of the brain.[28]

(4) Relatively prolonged pneumococcal infections (6–9 days) did not induce tolerance to pyrogen,[4] thus virtually eliminating the possibility that a circulating bacterial pyrogen is involved in the pathogenesis of pneumococcal fever.

The fact that bacterial endotoxins are active in minute quantities when injected intrathecally[25] suggests that pyrogenic products of the invading pneumococci might gain access to the subarachnoid space and thus contribute to the fever. This possibility also appears to be excluded; since bacterial pyrogen was not detected in pneumococcal cultures or in the peritoneal exudate, the thoracic-duct lymph, or the blood-stream,[26 35] it is inconceivable that it could be present in the spinal fluid.

In experimental streptococcal cellulitis the situation is complicated by the fact that a bacterial pyrogen can be extracted from β-hæmolytic streptococcal cells.[44] However, the endotoxic activity of streptococcal extracts is relatively low,[44] and in this infection the organisms do not invade the blood-stream.[28] Here again the circulating pyrogen which appears to cause the fever produces a more rapid febrile response than do bacterial pyrogens. Furthermore, unlike bacterial pyrogen, it is uninfluenced by tolerance and acts directly on the central nervous system via the circulation.[28]

Even in experimental infections caused by *Escherichia coli*, which is known to possess a powerful pyrogenic endotoxin, there is at present no evidence that the endotoxin is directly involved in the production of fever. On the contrary, *Esch. coli* infections of 7 or 8 days' duration, like pneumococcal infections, do not produce tolerance to bacterial pyrogens.[4] Were the endotoxin to reach the spinal fluid in extracranial *Esch. coli* infections, it would still have to traverse the blood-stream. In so doing it would certainly be expected to cause some degree of pyrogen tolerance.

Thus the conclusion appears justified that the fever of most, if not all, acute bacterial infections which give rise to predominantly granulocytic exudates and do not directly involve the central nervous system are caused by a common factor—i.e., a circulating endogenous pyrogen derived from polymorphonuclear leucocytes and analogous to the bloodborne substance found in the sera of rabbits with pneumococcal peritonitis and streptococcal cellulitis.[28]

The further possibility that similar circulating endogenous pyrogens, derived from leucocytes or other inflammatory cells, may cause an even wider variety of pyrexia is suggested by the fact that inflammation is common to many pyrexial states, including those resulting from viral infections, vascular lesions, hypersensitivity reactions, and neoplastic diseases.[48] Pertinent to this more general hypothesis is the recent observation of Atkins [28] that the febrile response to intravenous injection of influenzal virus is directly related to the presence of a circulating endogenous pyrogen which is indistinguishable from leucocytic pyrogen. Whether this newly identified factor is derived from polymorphonuclear leucocytes or from some other cellular source remains to be determined. Equally important is Atkins' demonstration (personal communication) of a similar substance in the blood-stream of animals with fever induced by tuberculin hypersensitivity.[43] Both these findings, together with those already mentioned relating to pneumococcal and streptococcal infections,[28] support the general theory that endogenous pyrogens derived from inflammatory exudates play a central role in the pathogenesis of many forms of fever.

Studies in man [17 20 42] further support this concept. Of particular significance is the fact that human serum and plasma have been shown to inactivate bacterial endotoxin.[20 22 23‡] This inactivation may be related to the release of phosphorus from the endotoxin molecule.[40] When, however, endotoxin is added to human whole

‡ Endotoxin is also inactivated by rabbit serum when incubated at 37°C for more than a few hours.[16]

blood or to plasma containing leucocytes, incubation for 3 hours results in the formation of a pyrogenic substance which apparently possesses all the biological properties of endogenous pyrogen.[42] Since leucocytes are necessary in the system for production of the pyrogen,[17] and since its properties are indistinguishable from those of leucocytic pyrogen,[42] the inference may be drawn that the pyrogen is produced by the leucocytes. A difference from the observations made with rabbit leucocytes [25] is that easily demonstrable amounts of the human endogenous pyrogen have been obtained only when the leucocytes have been exposed to the injurious action of endotoxin.[39] This difference, however, may be merely quantitative.

The term " endogenous pyrogen " used in this and previous reports [1 2 26–28 46 47] refers to fever-producing substances which are apparently derived from sources within the body. Clearly, leucocytic pyrogen [26 42] fits this definition, as do the pyrogenic factors contained in the blood-streams of rabbits with pyrexia caused either by injections of typhoid vaccine [1 2] § or by active pneumococcal and streptococcal infections.[28] Unfortunately the same term has been applied by Grant and Whalen [21] to the pyrogenic factor which results from the interaction of bacterial pyrogens and serum. Although its use to designate the pyrogen-serum product is justifiable on the grounds that the interaction may occur in the circulation, the resulting pyrogenic factor has been shown to form rapidly in vitro [18] and obviously involves a component which was originally exogenous. For these reasons, to avoid confusion, it appears preferable to call the bacterial pyrogen-serum substance by another name. The pyrogenic tissue polysaccharides of Landy and Shear [20] also qualify by definition as " endogenous ", but they were obtained only by relatively drastic procedures of chemical extraction.[20] As emphasised by Landy and Shear, the extracted polysaccharides appear to be active " only when they are released from their native state of firm combination with other cellular components ",[20] and there is no evidence that they act directly as pyrogens in the intact host, even under conditions of disease.

The endogenous pyrogens, as here defined, are biologically indistinguishable from leucocytic pyrogen (see table). Indeed there are numerous reasons, already reviewed, for believing that the circulating endogenous factor which appears to cause the fever of acute bacterial infections,[28] and that present in the blood during endotoxin-induced fever,[1 2] are both derived from polymorphonuclear leucocytes.[26] All attempts to demonstrate similar endogenous pyrogens in saline extracts of other body cells have so far failed.[5 9] It is still possible, however, that cells other than granulocytes can produce endogenous pyrogen. If these cells could be identified, the fever seen in agranulocytosis and in diseases in which polymorphonuclear leucocytes do not appear to play a prominent role—e.g., granulomata and viral infections—might be more readily explained. On the other hand, it is not inconceivable that, even in these situations, enough leucocytes are affected in the vast extravascular granulocytic stores of the body [31] to explain the release of endogenous pyrogen. Further experimental studies are needed to clarify these points.

Chemistry

Since it is evident that leucocytic pyrogen is at least one of the endogenous factors directly responsible for fever, its chemical identity is of great interest. Besides being inactivated when heated to 90°C for 30 minutes (at pH 7·2), leucocytic pyrogen is known to be non-dialysable through ' Cellophane '. It has also been reported to be resistant to the actions of trypsin, chymotrypsin, and ribonuclease, and to be unaffected by pH changes ranging from 2·0 to 10·5. Significant pyrogenicity has been demonstrated in preparations containing 0·76 mg. of protein and 0·054 mg. of polysaccharide.[10] Clearly, additional chemical data are needed, and studies designed to procure them are in progress.

§ Endogenous pyrogen is easily demonstrable in the sera of such animals 2 hours after inoculation of the vaccine, at which time the bacterial pyrogen contained in the originally injected vaccine is no longer detectable in the circulation.[2]

Summary

There is now strong experimental evidence that endogenous pyrogen derived from polymorphonuclear leucocytes in inflammatory exudates plays a central role in the pathogenesis of many kinds of fever. Leucocytes in granulocytic exudates release the endogenous pyrogen into the surrounding medium while still functionally active.

During the febrile phase of experimental pneumococcal peritonitis the pyrogen has been found not only in the peritoneal exudate and the thoracic-duct lymph but also in the blood-stream.

An endogenous pyrogen indistinguishable from leucocytic pyrogen has likewise been detected in the sera of rabbits with pyrexia resulting from acute streptococcal cellulitis, from tuberculin hypersensitivity, and from the intravenous injection of typhoid vaccine and of influenzal virus.

This recently identified circulating factor acts directly on the thermoregulatory centres of the brain.

Its biological properties differ distinctly from those of bacterial pyrogens, pyrexin, and the pyrogenic polysaccharides which can be chemically extracted from normal tissues. None of the latter appears to be the direct cause of the fever seen in extracranial bacterial infections.

Despite the progress achieved in elucidating the pathogenesis of fever, two major problems remain unsolved: (1) the chemical identity of leucocytic pyrogen; and (2) the possibility that cells other than polymorphonuclear leucocytes may be able to elaborate a similar, if not identical, fever-producing factor.

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GROSS DIGITAL CLUBBING AND EXOPHTHALMIC OPHTHALMOPLEGIA IN THYROID DISORDERS

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IT is a sobering thought that the pathogenesis of such a common and easily recognisable physical sign as clubbing of the fingers should still not be fully understood. As early as the 5th century B.C., curving of the finger nails in a woman with an empyema was recorded by Hippocrates. Yet the reason why digital clubbing occurs remains a matter of conjecture and controversy.

Clubbing of the fingers and hypertrophic pulmonary osteoarthropathy are now generally ascribed either to peripheral anoxia or to a disturbance of endocrine function rather than to the "toxins" of earlier workers (*Lancet* 1955). Nevertheless very few textbooks on clinical medicine or on endocrinology mention the association of finger clubbing with disorders of the endocrine glands. For example, although there are some isolated references to the fact that acropachy may, on rare occasions, occur in postoperative myxœdema, far greater emphasis is laid on the fact that the nails usually become atrophic and unduly brittle in this condition.

Digital Clubbing, Exophthalmic Ophthalmoplegia, and Hypothyroidism

Thomas (1933) reported a man, aged 22, who first observed curving of his finger nails about eight months after partial thyroidectomy for exophthalmic goitre. Sixteen months later he was mildly myxœdematous and had œdema of the eyelids. There is no indication in the case-report whether the exophthalmos had progressed or diplopia had developed. Extreme clubbing of the fingers and enlargement of the hands and wrists were present. The toenails were normal. Radiography revealed tufting of the terminal phalanges and much subperiosteal formation of new bone; the sella turcica was normal.

Cushing (1937) described a further case. A negro, aged 37, first noticed that the tips of his fingers were becoming swollen eight months after subtotal thyroidectomy. He had severe digital clubbing, and radiography showed generalised hypertrophic pulmonary osteoarthropathy affecting his long bones and metacarpals. His basal metabolic rate was −24% compared with +55% before operation. As in the previous case, nothing is said about whether ophthalmoplegia had complicated the pre-existing exophthalmos.

Rynearson and Sacasa (1941) reported a man, aged 43, who became hypothyroid and developed clubbing of his fingers six weeks after partial thyroidectomy for thyrotoxicosis. Two years after the operation his exophthalmos had increased and he had brawny irregular non-pitting œdema of the lower half of his legs. His basal metabolic rate was −13%, and radiography showed subperiosteal thickening of his phalanges.

Greene (1951) described a man, aged 74, with hypothyroidism, malignant exophthalmos, and gross clubbing of the fingers and toes, who at the age of 56 in 1932 had an enlarged thyroid gland, exophthalmos, an enlarged heart, and chronic bronchitis. He had no digital tremor or tachycardia. After treatment with potassium iodide the goitre disappeared. At this time his fingers were clubbed but, according to his relations, this only became severe seventeen years later, when progressive exophthalmos appeared. He also had pretibial thickening of his skin. Radiography of his chest showed emphysema; a bronchogram was normal. Radiography of his skull showed no abnormality; radiography of his hands and feet revealed the formation of new bone along the shafts of his phalanges and metacarpals.

This man died in 1951. A necropsy was done by Dr. A. B. Bratton, and I am indebted to Dr. Greene for sending me full details of the hitherto unpublished necropsy findings. In summary, there were considerable hypertrophy of the left ventricle, œdema of the lungs, and emphysema. A cystic adenoma was present in the left lobe of the thyroid gland, and microscopy revealed lymphocytic infiltration, massive fibrosis, and scanty colloid in the small residual nodules of thyroid epithelium. The suprarenal glands had abundant lipoid in the cortex and considerable lymphocytic infiltration of the medulla. There was an eosinophil chromophil adenoma of the anterior lobe of the pituitary gland.

Inch and Rolland (1953) reported 2 cases in which pretibial myxœdema and gross digital clubbing were associated with exophthalmic ophthalmoplegia. One case was in a woman who developed an exophthalmic goitre at the age of 36. Within nine months of partial thyroidectomy she had signs of hypothyroidism, ophthalmoplegia, pretibial myxœdema, and finger clubbing. The other case was in a man who became thyrotoxic at the age of 20. After X-irradiation of the thyroid gland he became euthyroid and developed exophthalmos with mild ophthalmoplegia. He was first seen by Inch and Rolland nineteen years later with considerable exophthalmos, some ophthalmoplegia, pretibial myxœdema, and gross finger clubbing. The patient did not know when the clubbing had begun to appear.

Analysis of these 6 case-reports reveals that the clinical features common to all were digital clubbing and exophthalmos. 5 patients were hypothyroid, and 1 was euthyroid. This hypothyroid or euthyroid state followed partial thyroidectomy or X-irradiation of the thyroid gland for thyrotoxicosis in 5 patients. In 1 case myxœdema was first noticed about seventeen years after the goitre had disappeared after treatment with potassium iodide.

Exophthalmic ophthalmoplegia was present in 4 cases, whereas in 2 (Thomas 1933, Cushing 1937) it is not said whether the pre-existing exophthalmos had increased or diplopia had developed. In 4 patients digital clubbing came on between six weeks and nine months after either partial thyroidectomy or X-irradiation of the thyroid gland and closely followed the symptoms of hypothyroidism. In 1 case the patient did not know when the clubbing had first appeared. In the other case, although the clubbing had appeared before the goitre had been treated with potassium iodide, it had only become severe seventeen years later, when hypothyroid symptoms and malignant exophthalmos had developed. Pretibial myxœdema was observed in 3 of the 6 cases.

A further case is now reported.

Case-reports

Case 1.—An engine driver, aged 56, was referred to the Bristol Eye Hospital in October, 1957, with three months' history of increasing prominence of his eyes. For three weeks

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he had had progressive swelling of his left upper eyelid and watering of the eye. During the preceding seven days he had had pain in his left eye and photophobia and could not close his eye completely. In 1929, at the age of 28, subtotal thyroidectomy followed by X-irradiation of the thyroid gland were undertaken for thyrotoxicosis of some eleven months' duration. The hospital records state that after this treatment the exophthalmos regressed somewhat and the patient regained his previous weight. For four months before be was seen at the Bristol Eye Hospital he had felt tired and been unduly sensitive to cold, and his skin had become rough and dry and his voice a little husky, and he was constipated. There was no apparent impairment of memory or of power to concentrate. For about twenty years up to the time of admission he had been driving a main-line express train.

On examination his speech was a little slow and slurred and his voice low-pitched. He had coarse features, a dry scaly skin, dry hair, and a puffy face. No circumscribed or pretibial myxœdema was found. Gross clubbing of his fingers and toes was present (fig. 1). There was neither pain nor swelling of his ankles, feet, or wrists. Marked bilateral exophthalmos (exophthalmometer: right eye 29 mm., left eye 28 mm.*) was present. Œdema and inflammation of his periorbital tissues and the infracorneal conjunctiva were severe. His left eye was lagophthalmic, with eversion of the lower lid, exposing œdematous conjunctiva and producing epiphora (fig. 2). He had no diplopia, but he had difficulty in looking upwards. His visual acuity was right 6/9, left 6/18; his ocular fundi and visual fields were normal. His cardiovascular system, chest, and abdomen revealed no abnormal physical signs.

Investigations and follow-up examination.—During his stay in hospital the patient's temperature was 96–98°F and pulse-rate 60–70. Blood-counts and liver-function tests were normal; his plasma-cholesterol level was 280 mg. per 100 ml.

* Since there appears to be a wide range of measurements made with a Hertel exophthalmometer in healthy people, the degree of exophthalmos is not given. For example, Brain and Turnbull (1938) state that the average normal reading is 12·5 mm., whereas Rundle and Wilson (1945) report the average values in controls measured by the same instrument as 16·9 ± 1·8 mm., with the upper limit of normal as high as 23·0 mm.

Fig. 1—Case 1: clubbing of fingers and toes.

Electrocardiography revealed flattening of the T waves in all leads. Radiography of his chest showed fibrotic changes in the anterior segment of the right upper lobe and bilateral basal emphysema. Bronchography showed all the main segmental bronchi in both lungs and no evidence of bronchiectasis. Radiography of his skull, hands, and long bones was normal, but there was periosteal new bone on the medial aspects of both first metatarsals (Dr. J. H. Middlemiss). Radioactive-iodine estimations showed that at four hours the total uptake was as low as 9% of the dose, and at forty-eight hours the protein-bound ^{131}I level in the plasma was 0·13% of the dose per litre, the values obtained being consistent with the clinical diagnosis of myxœdema. A left central and lateral tarsorrhaphy and a right lateral tarsorrhaphy were done as an emergency measure, and a course of X-irradiation to the orbits has now been given.

Fig. 2—Case 1: malignant exophthalmos. Left lateral and central and right lateral tarsorrhaphies had been done as emergency measure.

Comment.—There was no history or clinical evidence of pulmonary, cardiac, hepatic, or intestinal disease in this patient and no family history of clubbing of the fingers. Although the plain radiographs of his chest showed fibrotic changes in the anterior segment of the right upper lobe, bronchography showed no bronchiectasis. The patient and his wife both thought that the clubbing of his fingers had been present for only three or four months. In this patient, therefore, there was a definite association between the onset of digital clubbing, exophthalmic ophthalmoplegia, and clinical manifestations of hypothyroidism.

Digital Clubbing, Exophthalmic Ophthalmoplegia, and Thyrotoxicosis

Although it is well known that trophic disturbances leading to koilonychia may develop in thyrotoxicosis, Branwood (1949) stated that clubbing of the fingers is not seen in this condition. I have been unable to find any reference or case-report similar to case 2 (see below) describing the clinical triad of gross digital clubbing, exophthalmic ophthalmoplegia, and untreated active thyrotoxicosis.

Case 2.—A warehouseman, aged 54, was admitted to the Bristol Eye Hospital in October, 1956, with six months' history of nervousness, irritability, palpitations, and increasing prominence of his eyes. In spite of having a good appetite he had lost almost 2 stones in weight. During the previous four weeks he had had puffy eyelids. Pain in his eyes and photophobia had been present for three days.

On examination he was nervous and agitated. His skin was warm and moist, and a fine tremor of his fingers was present. His resting pulse-rate was 130, with normal rhythm. His blood-pressure was 180/95 mm. Hg. His thyroid gland was easily palpable and uniformly enlarged. A loud systolic bruit was audible over his neck. Bilateral proptosis (exophthalmo-

Fig. 3—Case 2: malignant exophthalmos.

meter: right eye 25 mm., left eye 26 mm.*) was present. Lid lag, lid retraction, and widening of the palpebral fissures were evident. His upper and lower eyelids were œdematous and inflamed, and chemosis was present (fig. 3). There was some weakness of elevation and abduction in both eyes, and the patient complained of double vision when attempting to look to the extreme left and right. His visual acuity was right 6/6, left 6/5; his ocular fundi and visual fields were normal. He had no pretibial myxœdema. He also had gross clubbing of his fingers and toes (fig. 4). He had no enlargement of his hands and feet and no pain or swelling of his ankles, feet, or wrists. His face showed no sign of acromegaly. He had some thickening and furrowing of his skin over his forehead. His heart, lungs, and abdomen were normal clinically.

Investigations.—Complete blood-counts, liver-function tests, and radiography of his thoracic inlet, chest, long bones, hands, and feet were all normal. Radiography of his skull showed no intracranial abnormality, and his sella turcica was normal. Radioactive-iodine measurements showed that the total uptake

Fig. 4—Case 2: clubbing of fingers and toes.

was 82% of the dose, at four hours, and at 48 hours the protein-bound ^{131}I level in the plasma was $1{\cdot}35 \pm 0{\cdot}08\%$ of the dose per litre, values consistent with thyrotoxicosis.

Progress.—Bilateral lateral tarsorrhaphies were done and the patient was transferred to the Bristol General Hospital for radioactive-iodine therapy. He became euthyroid and in twelve months there was definite improvement in his exophthalmos and ophthalmoplegia. His extreme digital clubbing has remained unchanged, and no signs of circumscribed myxœdema have appeared.

Comment.—In this patient there was no family history of digital clubbing and no evidence of cardiac, pulmonary, hepatic, or intestinal disease. Although the skin over his forehead appeared a little thickened and furrowed, he had no prominent skin folds on his cheeks, exaggeration of the normal nasolabial folds, or enlargement of his extremities, all of which are such characteristic features of pachydermoperiostosis (idiopathic osteoarthropathy) (Angel 1957). The patient had first noticed curving of his finger-nails about two or three months before he was seen at the Bristol Eye Hospital.

It therefore appears that the development of digital clubbing closely followed the onset of symptoms and signs of a toxic goitre and progressive exophthalmos. When the patient was first seen in October, 1956—six months after the onset of his thyrotoxic symptoms—gross digital clubbing, exophthalmic ophthalmoplegia, and signs of active thyrotoxicosis were present.

Discussion

Pretibial myxœdema—first described by a Bristol physician (Watson-Williams 1895)—and its association with exophthalmic ophthalmoplegia are now well recognised. The complete clinical triad with gross digital clubbing is evidently rare but apparently not so rare as the paucity of published reports suggests.

Analysis of the published case-reports shows that a definite association between the onset of acropachy, exophthalmic ophthalmoplegia, pretibial myxœdema, and hypothyroidism existed in 2 men (Rynearson and Sacasa 1941, Greene 1951) and 1 woman (Inch and Rolland 1953). In a further 3 cases reviewed the association between acropachy and exophthalmic ophthalmoplegia is not proved, because insufficient data about the time of onset of digital clubbing and the presence of malignant (as opposed to benign) exophthalmos is recorded. Levitt (1953) wrote that he had seen 8 such patients, but he gave no further clinical details.

In the present case 1 the development of severe digital clubbing and progressive exophthalmos with ophthalmoplegia closely followed the onset of classical symptoms and signs of myxœdema. In case 2 gross clubbing of the fingers and toes and exophthalmic ophthalmoplegia developed in a patient with a toxic goitre. No other case of severe digital clubbing in untreated active thyrotoxicosis seems to have been published. There were no signs of pretibial myxœdema in either of these 2 cases.

Clinical Manifestations of Pituitary Dysfunction

Exophthalmic ophthalmoplegia.—The concept expressed by many workers that exophthalmic ophthalmoplegia is due to overproduction of the thyroid-stimulating hormone (T.S.H.) of the anterior lobe of the pituitary gland has been challenged by Gilliland and Strudwick (1956). Using a new method of clinical assay of T.S.H. in the serum which would not be affected by the presence of

excess thyroid hormone, these workers found a high level of T.S.H. in most patients with spontaneous myxœdema and in cretins comparable with the raised level also obtained in 8 patients with thyrotoxicosis and severe eye signs. Further, the T.S.H. levels in 3 patients with exophthalmic ophthalmoplegia without thyrotoxicosis did not differ from those found in healthy controls. Gilliland and Strudwick therefore conclude that oversecretion of T.S.H. is not the sole cause of exophthalmos.

The supposed existence of an " exophthalmos-producing " hormone, possibly also of pituitary origin, as a separate entity from T.S.H. is supported by the findings of Querido and Lameyer (1956). In 18 thyrotoxic patients there was no significant difference between the levels of T.S.H. in the serum of 9 patients without serious eye signs and in that of 7 with serious eye signs. Further, the circulating T.S.H. levels were repeatedly low in 1 euthyroid patient who developed malignant exophthalmos after partial thyroidectomy, and were very high in another with only slight proptosis, pretibial myxœdema, and postoperative hypothyroidism. Thus there appears to be no direct correlation between the levels of T.S.H. in the serum and the presence and degree of exophthalmos.

Digital clubbing.—The question now to be considered is whether acropachy can ever be regarded as a clinical manifestation of pituitary dysfunction.

Bloom (1948) reported chronic hypertrophic pulmonary osteoarthropathy and gynæcomastia in a man with a carcinoma of the bronchus. He found metastases in the anterior lobe of the pituitary gland at necropsy and suggested that these had excited the production of anterior-lobe hormones in sufficient quantity to produce the bone changes, digital clubbing, and gynæcomastia which had developed during the course of the disease. The regression of digital clubbing which often occurs after lung resection clearly excludes stimulation of the hypophysis as a common cause, and Flavell (1956) has shown that severing the vagus nerve on the same side as the affected lung also completely reverses the signs of osteoarthropathy.

On the other hand, Fried (1943) has presented evidence in support of dyspituitarism as an ætiological factor in some cases. He described the development of chronic hypertrophic pulmonary osteoarthropathy, clubbing of the fingers, and clinical and radiological features of acromegaly in 4 patients with a bronchogenic carcinoma. Ellman (1953) and Järvinen and Kumlin (1954) also reported similar clinical findings in 4 patients with the same neoplastic condition. Hyperplasia of the eosinophil cells of the anterior lobe of the pituitary gland without any metastatic involvement of the endocrine glands was found in all 4 patients on whom postmortem examinations were performed.

Levitt (1954) wrote:

" The presence of pulmonary osteo-arthropathy in a patient with severe malignant exophthalmos and localised œdema of the legs support the view that the pituitary gland is closely associated with this phenomenon. . . . The associated eosinophil hyperplasia present in the pituitary gland adds further support to the view that the growth factor is very closely allied to the proliferative thyroid hormone."

The hitherto unpublished necropsy findings in the case presented by Greene (1951) merit particular emphasis. This male patient, with hypothyroidism, gross digital clubbing, malignant exophthalmos, and pretibial myxœdema, died at the age of 76. Some seventeen years before he was first seen by Dr. Greene he had been treated with potassium iodine for an apparently non-toxic goitre, and after this treatment the thyroid enlargement had disappeared. Necropsy showed severe thickening of the fingers and toes and formation of new bone along the shafts of the metacarpals. Pulmonary congestion was present, but there were no signs of a bronchogenic carcinoma. Massive fibrosis of the thyroid gland and an eosinophil chromophil adenoma of the anterior lobe of the pituitary gland were also found.

Conclusions

The role of the pituitary gland in the production of exophthalmic ophthalmoplegia and in the pathogenesis of digital clubbing has been studied and reviewed by many workers.

The concept of an " exophthalmos-producing " hormone as a separate entity from the thyroid-stimulating hormone of the pituitary gland is now widely held. In the light of clinical and necropsy findings the development of acropachy and chronic hypertrophic pulmonary osteoarthropathy in some patients with a bronchogenic carcinoma has been ascribed to a disturbance of pituitary function. In this connection the necropsy findings are of particular interest in 2 patients with either medically induced or postoperative hypothyroidism associated with malignant exophthalmos, pretibial myxœdema, and gross digital clubbing: one patient had an eosinophil chromophil adenoma of the pituitary gland; the other had eosinophil hyperplasia of the anterior lobe of the pituitary gland.

The association of acropachy and exophthalmic ophthalmoplegia in patients with either postoperative or medically induced myxœdema is not so rare as might be expected from the paucity of published reports. On the other hand, the development of severe digital clubbing and exophthalmic ophthalmoplegia in untreated active thyrotoxicosis (case 2) does not appear to have been previously described.

The fact that gross digital clubbing is now reported in association with exophthalmic ophthalmoplegia in hyperthyroid, as well as in induced euthyroid and hypothyroid states, adds further support to the view that this syndrome, with or without pretibial myxœdema, is a clinical manifestation of pituitary dysfunction.

I am indebted to Mr. C. A. Brown and Dr. A. M. G. Campbell for permission to publish the two case-reports; Dr. J. L. James for helpful criticism and advice; and Mr. F. A. Godman, of the department of photography, University of Bristol, for the photographs.

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INTRINSIC-FACTOR-INHIBITING SUBSTANCE IN SERUM OF ORALLY TREATED PATIENTS WITH PERNICIOUS ANÆMIA

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PERNICIOUS anæmia has been extensively treated with intrinsic factor for more than twenty-five years, especially in the Scandinavian countries. Formerly the preparations consisted of more or less crude dried hog gastric pylorus, but in the past five or six years a new type of oral preparation has become very popular: purified hog pyloric mucosa plus vitamin B_{12}. It has been shown that only 100 mg. of hog pyloric mucosa causes substantial absorption of vitamin B_{12} in pernicious anæmia, and such preparations administered initially almost always produce complete remission. But in prolonged treatment with preparations of this type a considerable proportion of the patients relapse, and several have shown myelopathy—even without hæmatological relapse in the peripheral blood. (Blackburn et al. 1955, Meulengracht 1955, Nørregaard 1955, Bastrup-Madsen 1957.)

TABLE I—URINARY EXCRETION IN SCHILLING TEST PERFORMED WITHOUT INTRINSIC FACTOR, WITH HOG INTRINSIC FACTOR ALONE, AND WITH HOG INTRINSIC FACTOR MIXED WITH 50 ML. SERUM FROM HEALTHY PERSONS. FIGURES ARE PERCENTAGES OF ADMINISTERED ^{60}CO VITAMIN B_{12} EXCRETED IN URINE IN 24 HOURS

Intrinsic factor		
None	100 mg. hog pyloric mucosa	100 mg. hog pyloric mucosa + 50 ml. serum
0·7	15·7	16·3
0·7	15·7	17·0
0·7	15·7	10·4
0	26·6	21·6
0	19·1	27·5
2·2	12·2	8·8
0	21·2	32·0
2·6	18·0	16·1
7·1	28·2	15·3
7·1	28·2	21·0
0	16·4	10·8
0	14·0	18·7
0·7	20·7	16·8
0	16·4	16·5

The cause of the failure of these newer oral preparations is a block in the intestinal absorption of vitamin B_{12} with hog pyloric mucosa as intrinsic factor; the block is not present when homologous intrinsic factor is administered (Schwartz et al. 1957). This intestinal block has been confirmed by several workers (Berlin et al. 1957, Killander 1957, Lowenstein et al. 1957, Allgén and Tomenius 1958, Stokes and Pitney 1958); but its cause has not been found so far. The block may be due to some sort of sensitisation; two groups found no evidence of immunity in such patients, but they did not state how their investigation was carried out. (Stokes and Pitney 1958, Adams 1958.) Recently an antibody to Castle's intrinsic factor was reported by Taylor and Morton (1958). They immunised rabbits with intrinsic-factor preparations from man and from pig pylorus and found in the serum of the treated rabbits a substance inhibiting human and pig intrinsic factor respectively.

As part of investigations in this hospital into the cause of the intestinal block in orally treated patients with pernicious anæmia, several sera from healthy persons and patients with pernicious anæmia were examined for antibody against intrinsic factor.

Methods

The Schilling (urinary excretion) test was used throughout, 0·5 μg. ^{60}Co vitamin B_{12} (with 0·1 μC) was administeted by mouth, and 2 hours later 1 mg. unlabelled vitamin B_{12} intramuscularly. ^{60}Co vitamin B_{12} excretion was determined in 24-hour specimens of urine.

The patients all had typical pernicious anæmia with a low (0–7·1%) ^{60}Co vitamin B_{12} excretion when tested without intrinsic factor, and a normal ^{60}Co vitamin B_{12} excretion (in this series 12·2–28·2%) with 100 mg. hog pyloric mucosa.

TABLE II—URINARY EXCRETION IN SCHILLING TEST PERFORMED WITHOUT INTRINSIC FACTOR, WITH HOG INTRINSIC FACTOR ALONE, AND WITH HOG INTRINSIC FACTOR MIXED WITH 50 ML. SERUM FROM PATIENTS WITH UNTREATED PERNICIOUS ANÆMIA. FIGURES ARE PERCENTAGES OF ADMINISTERED ^{60}CO VITAMIN B_{12} EXCRETED IN URINE IN 24 HOURS

Intrinsic factor		
None	100 mg. hog pyloric mucosa	100 mg. hog pyloric mucosa + 50 ml. serum
0·7	20·7	18·2
0	21·2	18·6
0	16·0	14·9
0	16·4	13·8
0	14·0	15·1
0	16·4	17·7

Serum from healthy persons and four groups of patients with pernicious anæmia was investigated: (1) untreated pernicious anæmia, (2) pernicious anæmia treated for 1–5 years with oral preparations of vitamin B_{12} plus hog pyloric mucosa, (3) pernicious anæmia treated orally with a crude stomach preparation ('Pylorin-Exopylorin'), (4) pernicious anæmia treated by injection. 50 ml. of serum was used in all experiments.

The test for antibody against intrinsic factor was carried out as follows: 100 mg. hog pyloric mucosa was mixed with a small amount of water and then with 50 ml. serum at room temperature. Ten minutes later the mixture was given with the test dose of ^{60}Co vitamin B_{12}.

Results

The results are shown in tables I–IV.

Serum from healthy persons (table I) and patients with untreated pernicious anæmia (table II) does not contain any intrinsic-factor-inhibiting substance.

Sera from 21 patients with pernicious anæmia treated orally for more than a year with preparations of vitamin

TABLE III—URINARY EXCRETION IN SCHILLING TEST PERFORMED WITHOUT INTRINSIC FACTOR, WITH HOG INTRINSIC FACTOR ALONE, AND WITH HOG INTRINSIC FACTOR MIXED WITH 50 ML. SERUM FROM PATIENTS WITH PERNICIOUS ANÆMIA TREATED ORALLY WITH PREPARATIONS OF VITAMIN B_{12} PLUS HOG PYLORIC MUCOSA (BENDOGEN, CYCOPLEX). FIGURES ARE PERCENTAGES OF ADMINISTERED ^{60}CO VITAMIN B_{12} EXCRETED IN URINE IN 24 HOURS

Intrinsic factor		
None	100 mg. hog pyloric mucosa	100 mg. hog pyloric mucosa + 50 ml. serum
0·7	15·7	0·3
0·7	15·7	1·0
4·4	15·3	1·4
0·7	20·7	1·4
0·7	15·7	1·6
2·6	18·0	3·7
0·7	15·7	4·2
2·2	12·2	4·3
0	16·4	4·6
0	26·6	5·4
2·6	18·0	7·5
0·7	15·7	7·6
6·9	19·8	7·9
7·1	28·2	8·1
7·1	28·2	8·3
0·7	15·7	11·5
0	26·6	11·8
0	14·0	12·3
0	16·4	15·9
0	16·4	17·0
0	21·2	22·6

TABLE IV—URINARY EXCRETION IN SCHILLING TEST PERFORMED WITHOUT INTRINSIC FACTOR, WITH HOG INTRINSIC FACTOR ALONE, AND WITH HOG INTRINSIC FACTOR MIXED WITH 50 ML. SERUM FROM PATIENTS WITH PERNICIOUS ANÆMIA TREATED ORALLY WITH A CRUDE STOMACH PREPARATION. FIGURES ARE PERCENTAGES OF ADMINISTERED ^{60}Co VITAMIN B_{12} EXCRETED IN URINE IN 24 HOURS

Intrinsic factor		
None	100 mg. hog pyloric mucosa	100 mg. hog pyloric mucosa + 50 ml. serum
0·5	15·7	1·4
0	14·0	1·4
0	14·0	2·2
0	16·4	12·9
0	20·7	10·6
0	14·0	18·4

B_{12} plus hog pyloric mucosa were investigated (table III). 16 of these sera inhibited the intrinsic-factor activity—in several cases almost completely. 13 of these 16 patients were investigated with ^{60}Co vitamin B_{21} and 100 mg. hog pyloric mucosa, and all were found to have a blocked intestinal absorption; 3 were not investigated, but in at least 1 of these patients absorption was probably blocked (serum-vitamin-B_{12} 32 μμg. per ml. after two years' treatment).

Of the 5 patients without intrinsic factor antibody in their serum, 3 were investigated; in 2 blockade was found, and the 3rd had normal vitamin-B_{12} absorption.

Serum from 6 patients with pernicious anæmia, treated orally for some time (six months to twenty years) with crude stomach preparations, showed gross inhibitory activity in 3 cases (table IV). The intestinal absorption was investigated in all 6 patients; 1 had a slightly reduced absorption (8·7% excretion with the Schilling test), whereas in the other 5 the absorption was normal.

Serum from 2 patients treated by injection showed no intrinsic-factor-inhibiting activity.

In some cases the experiments were repeated with the same sera. ^{60}Co vitamin B_{12} and hog pyloric mucosa were mixed 10 minutes before the addition of serum. The intrinsic-factor-inhibiting activity was found unaltered by this procedure (probably indicating that it is directed against the vitamin B_{12} plus intrinsic factor).

3 sera known to inhibit hog pyloric mucosa activity were tested in the same way, using human fundus mucosa as intrinsic factor. In 2 cases there was pronounced inhibiting activity against this homologous intrinsic factor.

Discussion

Intrinsic-factor-inhibiting activity in sera from patients with pernicious anæmia treated orally has not previously been reported. In order to examine as many sera as possible it was decided not to change the procedure in this investigation. Further studies, especially serological, are necessary. Possibly this intrinsic-factor-inhibiting substance is analogous with the intrinsic-factor-antibody produced experimentally in rabbits by Taylor and Morton (1958).

It is reasonable to assume that it is produced by the oral treatment, and it may partly explain why so many patients with pernicious anæmia, treated orally with vitamin B_{12} plus hog pyloric mucosa, develop a more or less blocked intestinal absorption of vitamin B_{12}. But this intrinsic-factor-inhibiting activity cannot alone explain the intestinal blockade. Patients treated with crude pig stomach preparations can have a quite normal intestinal vitamin-B_{12} absorption with hog pyloric mucosa and considerable intrinsic-factor-inhibiting activity in their serum. Furthermore the inhibiting activity was found to operate against human intrinsic factor.

Summary

Intrinsic-factor-inhibiting activity was found in a considerable proportion of sera from patients with pernicious anæmia treated orally. Serum from healthy persons and patients with untreated pernicious anæmia contained no such activity.

As intestinal absorption of vitamin B_{12} proved to be normal in some cases with inhibiting activity in the serum, and as the intrinsic-factor-inhibiting activity was shown to operate also against human intrinsic factor, such activity is probably not the sole cause of the intestinal blockade following long-continued oral treatment of pernicious anæmia.

I wish to thank Medicinalco, Ltd., of Copenhagen, for liberal supplies of intrinsic factor. This study was supported by the Statens Videnskabsfond, University of Copenhagen.

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FACIAL SINUSES SECONDARY TO PULMONARY TUBERCULOSIS

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IN three cases referred to us for the treatment of discharging sinuses on the face the lesions were found to be secondary to pulmonary tuberculosis. We know of only one such case (Oppenheim et al. 1950) previously reported.

Case-reports

Case 1.—A man, aged 33, had had an "abscess" in the left upper premolar region, 8 months previously. This was incised externally, but continued to discharge through a sinus. He had recently noted dyspnœa and a cough.

On the left cheek, about $1^1/_2$ in. distal to the angle of the mouth, was a depressed scar surrounding a sinus from which watery straw-coloured pus was discharging. Below the outer canthus of the left eye was a healed sinus with surrounding scar tissue, the centre of which was fluctuant (fig. 1). The dental condition was poor. A thick fibrous band was palpable in the buccal sulcus running from the alveolus in the /45 region to the cheek. Roots of the /45 teeth were present,

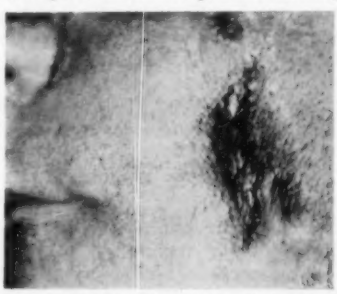

Fig. 1—Case 1. Chronically discharging facial sinus.

and radiographs showed rarefaction round the apices.

Staphylococcus albus and *aureus*, sensitive to penicillin, were cultured from pus from the sinus; no actinomyces were seen.

Intramuscular penicillin was given. All his teeth were removed, under a general anæsthetic, and the sinus on the cheek was explored: it appeared to end in the alveolar bone in the /45 region. No healing of the sinus took place, and cultures a week later produced *Staph. albus*, sensitive only to chloramphenicol. This antibiotic was now given in place of penicillin.

Fig. 2—Case 1. Sinuses healed after systemic treatment for pulmonary tuberculosis.

The temperature charts showed a " swinging " pattern like that seen in a tuberculous infection. Radiographs of the chest showed effusion at the base of both lungs and granular mottling throughout both lung fields, with some cavitation at the apices, suggestive of pulmonary tuberculosis. The sputum contained acid- and alcohol-fast bacilli, and pus from the sinus yielded tubercle bacilli, in pure culture.

When the patient was seen 12 months later, after medical treatment, the sinuses had healed and the scarring was much reduced (fig. 2).

Case 2.—A man, aged 22, was referred for a submandibular swelling. 4 weeks previously, the tooth had been extracted because of an acute alveolar abscess. The submandibular swelling had then increased in size, and his doctor had incised and drained it, since when it had been discharging.

Midway along the left mandible and below its lower border was a fluctuant area, about 2 cm. in diameter, surrounded by an area of fibrous tissue. The overlying skin was hyperæmic, and there were signs of a partially healed sinus. There was a second smaller swelling below the main area, and slight left submandibular adenitis. No intra-oral abnormalities were noted; the /7 socket was healing normally.

The sinus in the left submandibular region was reopened, and produced watery straw-coloured pus. Radiographs of the left mandible showed no lesion. Cultures of the discharge grew coagulase-negative staphylococci sensitive to penicillin.

Penicillin was given, but after a week there was little change in the condition. Accordingly, under general anæsthesia the sinus and the surrounding scar tissue was excised. A mass of granulation tissue was found with finger-like extensions; this was removed and the wound closed in layers. 14 days after operation a watery yellow discharge was coming from the two suture holes. At this stage tuberculosis was diagnosed in case 1, and in view of the similarity of his lesions, the second patient was also referred for a chest radiograph, which revealed a tuberculous appearance in the left lung. With appropriate medical treatment, the sinuses rapidly healed.

Fig. 3—Case 3. Chronically discharging sinus in the left submental region.

Case 3.—A man, aged 33, had a fracture of the right mandible involving an unerupted premolar tooth. Splints were applied by means of peralveolar and circumferential wires; fixation was achieved and maintained for 6 weeks; and union took place.

5 months later he returned with a discharging sinus in the left submental region (fig. 3). It had begun a week earlier as a painless swelling, which had increased in size, burst, and drained extraorally, with persistent discharge.

A swelling about $^3/_4$ in. in diameter was present in the left submental region. Pressure produced watery pus. The sinus coincided with the puncture hole that had been made in the skin to pass the circumferential wire. No intra-oral abnormalities were noted, and radiographs of the left mandible revealed no lesion.

Again the striking similarity of the lesion to that in case 1 prompted us to order an immediate chest radiograph, and this showed infiltration of the right and left upper and mid zones of the lungs. Bilateral cavitation was evident, and the sputum contained acid- and alcohol-fast bacilli. With treatment of his pulmonary tuberculosis, the submental lesion healed, and after 17 weeks there was only a scar (fig. 4).

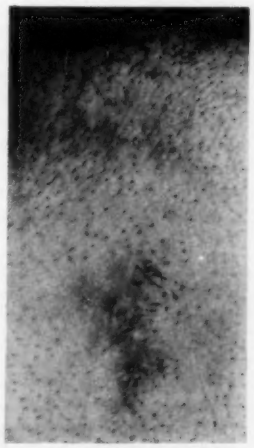

Fig. 4—Case 3. Sinus healed after systemic treatment for pulmonary tuberculosis.

Discussion

Tuberculous ulceration of the mouth may be primary or secondary. Secondary infection is more common; Cameron (1939) quoted an incidence of 1 case of ulceration in 1892 cases of pulmonary tuberculosis. The small numbers of cases suggest that the tissues of the oral cavity offer resistance to tuberculous infection. The explanation of this might be: (1) resistance of epithelium to the invading organisms; (2) protective and germicidal action of saliva; (3) rich blood-supply of the region; (4) constant movements of the tongue and cheeks, preventing long contact with the bacilli; or (5) antagonistic action of various bacteria to one another.

Chapotel (1930) wrote that only 50 cases of tuberculosis of the mandible had been reported up to 1922, and it was always associated with tuberculosis elsewhere. He suggested the following pathways by which infection reached the jaws: (1) from a tuberculous lesion of the gingivæ; (2) from infected sputum through the gingival tissues during tooth eruption; and (3) hæmatogenous spread.

Port and Euler (1951) thought that spread of tubercle bacilli to the jaw is more likely to be hæmatogenous than via a carious tooth; they cited the incidence of tuberculous infection of the zygomatic process, despite its relative great distance from the teeth.

Meng (1940) described 14 mandibular bone lesions, in 10 of which the chest was studied radiographically and revealed pulmonary tuberculosis.

60% of Chapotel's patients were under the age of 15, whereas Meng's patients varied in age from 4 to 48, 11 being between 10 and 30. Pilcher and Trauner's (1948) findings were similar to Chapotel's.

Partsch (1904), Darlington and Salman (1937), Gornouec (1939), and Brodsky (1942) demonstrated tubercle bacilli in the

periapical tissues of a tooth. Infection of sockets following extractions has occurred in patients with pulmonary tuberculosis (Burman and Jonsson 1935).

Oppenheim et al. (1950) reported one case of pulmonary tuberculosis where a fistula arose from the buccal mucosa through the skin of the cheek.

There is a similarity in our three cases. The first two patients complained of a " dental abscess ", and the third a swelling similar to a dental infection, as the initial symptom. None had pain. The discharging sinuses had the chronicity and lack of inflammatory symptoms of a tuberculous " cold abscess ". The sinuses and discharge were strikingly similar, together with an abnormal amount of fibrous tissue, especially in the first two cases.

It can be assumed that the lesions of the jaws were secondary to those in the lungs; but the route of infection is debatable. In cases 1 and 2 retained roots and carious teeth were present, allowing ingress of bacilli. In case 1 the tubercle bacilli in the sputum could have entered via the retained roots or through the blood-stream, and secondarily infecting a non-specific granuloma. In case 2 infection could have followed the extraction, if it was not already present. In case 3, we think, tubercle bacilli from the sputum tracked down the circumferential wire to the soft tissues. From the removal of the wire 5 months elapsed before the lesion appeared in the left submental region.

In our cases infection spread by the sputum seems more likely than infection via the blood. The staphylococci in the discharge, presumably arising from infected teeth, initiated an abscess and a sinus which favoured the superimposition of tuberculous infection.

Three constant factors in our cases are:

They had active pulmonary tuberculosis.

Pathways from mucous membrane to skin existed and opened up a route of infection by sputum.

A typical and easily recognisable facial lesion developed.

The clinical picture suggests that the deeper dermal layers have relatively little resistance to tuberculous infection; for mucous membrane, bone, periosteum, overlying soft tissues and skin were subjected to the same infection but were unaffected. Except the dermal structures, all healed normally.

Summary and Conclusion

Three cases are reported in which investigation of sinuses associated with jaws led to the diagnosis of unsuspected pulmonary tuberculosis.

In the treatment of dental conditions care should be taken to prevent external sinus formation, and to maintain a healthy mouth during treatment, even if this necessitates extensive conservative treatment of the teeth and gums.

We are indebted to Dr. Henry B. Slater, chest physician of Ashton-under-Lyne, for advice and progress reports on cases 1 and 3. We also thank Miss J. L. Perry, of Crumpsall Hospital, Manchester, for the photographs.

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ANTIBIOTIC-RESISTANT STAPHYLOCOCCAL OUTBREAKS IN A MEDICAL AND A SURGICAL WARD

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OUTBREAKS of staphylococcal infection in hospital wards are now common. The two reported here are of special interest because in both cases the origin was traced to an infected patient admitted to the ward, and the strains isolated were resistant to erythromycin as well as to penicillin, streptomycin, and tetracycline.

The first outbreak was in a male medical ward. Although the epidemic strain was scattered through the ward it was responsible for no severe infection and was eliminated without closure of the ward.

The second outbreak, which was in a male surgical ward, was responsible for 11 infections, many of which were severe, and was controlled only by closing and disinfecting the ward.

Bacteriological Methods

Staphylococci from infections were isolated in the routine laboratory on blood-agar plates, and all coagulase-positive strains were kept for further investigation. Nutrient-agar plates containing phenolphthalein phosphate (Barber and Kuper 1951) were used for isolating staphylococci from nasal swabs, bedding, curtains, and the air of the wards. Phosphatase-positive colonies were tested for the production of coagulase, and coagulase-positive strains were kept for further investigation. Samples from bedding were taken by the sweep-plate technique of Blowers and Wallace (1955).

All coagulase-positive strains isolated in this way were tested for sensitivity to penicillin, streptomycin, tetracycline, chloramphenicol, erythromycin, and novobiocin by the ditch-plate method. The concentrations of antibiotics used in the ditch were for penicillin 10 units per ml., streptomycin 50 or 200 μg. per ml., chloramphenicol 50 μg. per ml., and tetracycline, erythromycin, and novobiocin 25 μg. per ml. The Oxford staphylococcus was streaked across each plate as a control. Strains were recorded as sensitive if they showed a degree of sensitivity similar to that of the Oxford staphylococcus, resistant if they grew up to or across the ditch, and partially resistant if there was an intermediate degree of inhibition.

Representative strains were phage-typed by the method of Williams and Rippon (1952) using 21 phages.

Outbreak in Medical Ward

This ward was first studied in November, 1957, as part of an investigation into the incidence of strains of *Staphylococcus pyogenes* in the hospital environment. Nasal swabs were taken from all the patients and staff, and sweep-plates were made from the bottom and one top blanket of each patient and from one curtain round each bed.

Antibiotic Sensitivity of Strains Isolated

The number of strains of *Staph. pyogenes* isolated and their sensitivity to antibiotics are given in table I, which shows that strains resistant to penicillin, streptomycin, tetracycline, and erythromycin were isolated from eight blankets, three curtains, and the nasal swabs of 3 patients. The bedding of 7 patients was involved, 4 of whom were not apparently harbouring this type of staphylococcus in their anterior nares. Where strains with other patterns

TABLE I—STRAINS OF STAPH. PYOGENES ISOLATED FROM MEDICAL WARD

Source	No. examined	Total*	Strains of *Staph. pyogenes* isolated				
			Sensitivity to penicillin, streptomycin, tetracycline, and erythromycin (in that order)				
			SSSS	RSSS	RSRS	RRRS	RRRR
Patients' nasal swabs	22	20 (*15*)	3	7	2	5	3
Blankets	46	20 (*17*)	..	6	1	5	8
Curtains	26	6 (*6*)	..	2	..	1	3
Staff nasal swabs ..	19	12 (*12*)	2	10	..	..	..

R, resistant. S, sensitive.
* Figures in parentheses show number of specimens yielding *Staph. pyogenes*.

of resistance to antibiotics were found in bedding, in most cases this was in association with nasal carriage. Strains resistant to more than one antibiotic were not isolated from any of the staff.

All the strains were also tested for sensitivity to chloramphenicol and novobiocin. All were sensitive to novobiocin, but 2 of the 14 erythromycin-resistant strains were also resistant to chloramphenicol, and 2 of the other erythromycin-resistant strains yielded chloramphenicol-resistant variants.

Phage-typing Results

Of the 14 erythromycin-resistant strains 13 were tested for sensitivity to bacteriophages and showed an identical pattern: 53/75/77+.

Of the strains resistant to penicillin, streptomycin, and tetracycline but sensitive to erythromycin 7 were found to be of five different types, all of group III. 21 strains resistant to penicillin only were of ten different types, comprising strains of each of the three main phage-groups.

Source and Spread of Epidemic Strain

It seems clear from the foregoing results that a single strain of staphylococcus resistant to penicillin, streptomycin, tetracycline, and erythromycin was spreading round the ward. The 7 patients whose bedding was infected were not confined to any one area. The blankets of 5 patients, including 2 of the 3 nasal carriers, yielded only a few *Staph. pyogenes*. The 6th patient (A) had a top blanket heavily contaminated with this organism, but no coagulase-positive staphylococci were isolated from his nose, his bottom blanket, or the curtain surrounding his bed. Subsequently he was found to have a facial dermatitis infected with the epidemic strain.

In the 7th patient a heavy growth of the organism was isolated from his nose, both blankets, and the curtain round his bed. He had eczema of one leg with a generalised infected sensitisation dermatitis, and a heavy growth of the epidemic strain was obtained from skin swabs. He had been in the ward six weeks and had been treated with prednisone and corticotrophin together with penicillin and streptomycin and later with tetracycline. For the last week he had been up for part of the day and allowed to wander round the ward. It seems almost certain that he was responsible for the dissemination of the erythromycin-resistant staphylococcus. There is, however, no evidence that he brought the organism into the ward with him. He had been in the hospital for two months earlier in the year and had attended as an outpatient for many months. He had not been treated with erythromycin.

Control

Although no infections had resulted from the dissemination of this staphylococcus, in view of its antibiotic resistant pattern it was considered highly dangerous, and steps were taken to eradicate it. The patient who disseminated the strain was discharged, and the 2 patients carrying the epidemic strain in the nose were treated with neomycin-bacitracin cream. All the bedding and curtains were changed, and the clean blankets supplied were treated with a quaternary ammonium compound ('Arquad'). The floor was thoroughly washed with cresol.

Five days later sweep-plates were again taken from two blankets and one curtain of each bed. *Staph. pyogenes* was isolated from no curtains and from the blankets of only two beds. From one of these, seven colonies of a strain resistant to penicillin, streptomycin, and tetracycline but sensitive to erythromycin were isolated. From the other bed the epidemic erythromycin-resistant strain was isolated. This bed was that of patient A, whose top blanket had previously yielded a heavy growth of this organism, although it was not isolated from the patient's nose. The patient, however, was found to have a mild dermatitis of his face, and swabs from this yielded a similar staphylococcus. After his discharge and his bedding had been superseded by arquad-treated blankets the strain disappeared from the ward and in the subsequent two months was never isolated from patients or bedding.

Outbreak in Surgical Ward

The staphylococcal outbreak (Oct. 26 to Dec. 28, 1957) in the surgical ward was very different from the one just described. A single strain of *Staph. pyogenes* of phage type 80 caused infections of which many were very severe and one fatal in 11 people, including 2 nurses and 1 surgeon (table II). In all the cases the strain was resistant to penicillin and tetracycline, sensitive or partially resistant to streptomycin, and sensitive to novobiocin. The sensitivity to erythromycin varied; this was almost certainly due to the fact that case 1, who initially was infected with an erythromycin-sensitive organism, yielded an erythromycin-resistant variant after treatment with this antibiotic (see below). In case 8 a chloramphenicol-resistant variant was isolated; this finding is unexplained.

Fatal Case

Attention was first drawn to the ward because a patient (table II, case 2) had died of a fulminating staphylococcal pneumonia.

TABLE II—INFECTIONS IN OUTBREAK IN SURGICAL WARD

Case no.	Bed no.	Date of isolation of *Staph. pyogenes*	Source	Sensitivity to				
				Penicillin	Streptomycin	Tetracycline	Chloramphenicol	Erythromycin
1	8	Oct. 28, 1957	Boil	R	S	R	S	S
		Nov. 18, ,,	Wound	R	PR	R	S	R
		Dec. 3, ,,	Inguinal abscess	R	PR	R	S	R
2	2	,, 3, ,,	Sputum	R	PR	R	S	R
3	1	,, 9, ,,	Boil	R	PR	R	S	R
4	Nurse	,, 9, ,,	Septic finger	R	PR	R	S	R
5	8	,, 11, ,,	Sputum	R	PR	R	S	R
		,, 12, ,,	Transfusion wound	R	PR	R	S	R
		,, 18, ,,	Amputation wound	R	PR	R	S	R
6	11	,, 18, ,,	Wound	R	PR	R	S	R
7	Nurse	,, 20, ,,	Septic finger	R	PR	R	S	R
8	23	,, 23, ,,	Wound	R	PR	R	R	R
9	Surgeon	,, 31, ,,	Abscess	R	S	R	S	S
10	3–11	,, 31, ,,	Sputum	R	PR	R	S	S
11*	14	Jan. 11, 1958	Sputum	R	PR	R	S	R

PR, partially resistant. R, resistant. S, sensitive.
* This patient had been transferred to another ward.

He had been admitted on Nov. 21, 1957, with acute intestinal obstruction. He was extremely ill from his abdominal condition and also had bronchitis. He was treated by aspiration and with intravenous fluids, penicillin, and streptomycin. A few days later he was considered fit for operation; volvulus of the cæcum with patchy gangrene was found but no generalised peritonitis. His cæcum, his appendix, and part of his ascending colon were excised, and an end-to-end anastomosis was made. A course of tetracycline was started.

After operation the patient made a remarkable recovery and was up and looking well when, on the eighth postoperative day, he developed acute respiratory symptoms with thick purulent sputum which was choking him. Tracheotomy gave temporary relief, but his condition rapidly deteriorated, and he died within forty-eight hours of the onset of respiratory symptoms.

Necropsy revealed extensive infection of his lungs, but the condition of his abdomen was satisfactory.

Source of Infection

About a month previously, on Oct. 26, a patient (table II, case 1) had been admitted to the ward with multiple septic spots and boils due to a strain of *Staph. pyogenes* resistant to penicillin and tetracycline, partially resistant to streptomycin, and sensitive to chloramphenicol, erythromycin, and novobiocin. He was treated with erythromycin alone 250 mg. six-hourly for seven days to clear up his skin sepsis. On the fifth day of this treatment a recurrent pilonidal sinus in his sacral region was excised. On Nov. 18, ten days after operation, his wound showed signs of infection, and pus from it yielded a strain of *Staph. pyogenes* resistant to erythromycin, penicillin, and tetracycline, and partially to streptomycin. A fortnight later he developed an inguinal abscess from which a similar staphylococcus was isolated.

Subsequent investigation showed that the erythromycin-sensitive *Staph. pyogenes* isolated from him on admission and the erythromycin-resistant strains isolated from the wound and the inguinal abscess some weeks later were all of the same phage type—type 80. It is therefore clear that the strain had developed resistance as a result of the seven days' treatment with erythromycin. Since the strain isolated from the fatal case of pneumonia was of the same phage type, it seemed probable that this patient (case 1) was the source of infection.

Staphylococci in Environment

Bedding.—Sweep-plates were taken from two blankets and one curtain of each bed on Dec. 5. Table III shows that *Staph. pyogenes* was isolated from the blankets of 13 patients and the curtains of 12; ten of these twenty-five strains were resistant to penicillin and tetracycline, and nine others to these two antibiotics and erythromycin. All the erythromycin-resistant strains, tested by bacteriophage, were type 80, and two of eight strains resistant to penicillin and tetracycline but not to erythromycin were also type 80.

TABLE III—STRAINS ISOLATED FROM BLANKETS AND CURTAINS IN OUTBREAK IN SURGICAL WARD

Date (1957)	—	Total	No. of beds with infected blankets and curtains			
			Antibiotic sensitivity of strains isolated			
			S to all tested	R to penicillin only	R to penicillin and tetracycline	R to penicillin, tetracycline, and erythromycin
Dec. 5	Blankets	13	2	2	4	5
	Curtains	12	1	1	6	4
ALL BLANKETS AND CURTAINS SUPERSEDED BY ARQUAD-TREATED FABRICS						
Dec. 16	Blankets	9	4	3	1	1
	Curtains	2	..	..	..	1
Dec. 30	Blankets	4	..	2	1	1
	Curtains	1	..	1	..	..

R, resistant. S, sensitive.

Staff carriers.—On Dec. 11 nasal swabs were taken from 10 nurses; 6 carried *Staph. pyogenes*; one of the strains was sensitive to all the antibiotics tested, four were resistant to penicillin alone, and one, from the ward sister, was resistant to penicillin, tetracycline, and erythromycin. This last strain was phage type 80. *Staph. pyogenes* was isolated from only two nasal swabs of 11 doctors studied, and in both instances the strain was resistant to penicillin alone.

Air samples.—With a slit-sampler three samples of air were taken from each of four widely separated sites in the ward into nutrient agar containing phenolphthalein phosphate and tetracycline 10 μg. per ml. The 100 c. ft. of air thus sampled yielded eleven colonies of *Staph. pyogenes* resistant to penicillin and tetracycline. Nine of these colonies were resistant to erythromycin, and those tested were all phage type 80.

Attempts to Control Infection

Case 1 was transferred to a side-ward, and the ward sister who carried the epidemic strain in her nose was treated with neomycin-bacitracin cream and permitted in the ward only when adequately masked. The blankets, counterpanes, and curtains from all the beds were changed on Dec. 6. For the blankets were substituted immediately blankets treated with a quaternary ammonium compound (arquad), and the curtains which had been removed were similarly treated and then returned to the ward. Ten days later, sweep-plates taken from the blankets and curtains of all the beds gave the results shown in table III, which shows that, although the number yielding *Staph. pyogenes* was very much smaller, one blanket and one curtain carried the strain resistant to penicillin, tetracycline, and erythromycin.

Table II shows that, during this ten-day period, 2 more patients and 1 nurse developed infections due to strains of the same phage type. Case 3, with a boil, had recovered from his operation and was discharged, and the nurse was sent off duty. Case 5 had a very severe staphylococcal pneumonia as well as infection of an amputation stump and a transfusion wound. He was transferred to a side-ward and treated with vancomycin, to which he made a dramatic response.

At this stage attempts were made to spray the floor and the lower part of the walls of the ward with a quaternary ammonium compound; but, when the same strain of staphylococcus had infected the wounds of 2 more patients and the finger of 1 other nurse, it was decided on Dec. 28 to close the ward. Before the ward was empty, 1 further patient developed a chest infection and 1 surgeon developed an axillary abscess. Finally 1 patient who had been transferred to a medical ward with pulmonary tuberculosis was found to be superinfected with the epidemic strain of staphylococcus.

Nasal Carrier State of Patients and Staff at Time of Ward Closure

The nasal carrier state of patients and staff at this stage is analysed in table IV, which shows that only 6 of 20 patients carried *Staph. pyogenes*, but in 2 the strains were resistant to penicillin, tetracycline, and erythromycin. Of 15 nurses studied 12 carried *Staph. pyogenes*: 10 a strain

TABLE IV—CARRIER STATE OF PATIENTS AND STAFF ON DEC. 30, 1957, IN OUTBREAK IN SURGICAL WARD

—	No. examined	No. carrying *Staph. pyogenes*				
		Total	Antibiotic sensitivity of strains isolated			
			S to all tested	R to penicillin only	R to penicillin and tetracycline	R to penicillin, tetracycline, and erythromycin
Patients	20	6	1	3	..	2
Nurses	15	12	..	10	1	1
Doctors	11	4	..	2	2	..
Domestics, porters, physiotherapy, and X-ray staff ..	26	9	6	3	..	..

resistant to penicillin alone, 1 to penicillin and tetracycline, and 1 to these two antibiotics and erythromycin. This last was not the ward sister but a nurse who, when tested on Dec. 11, was carrying a strain sensitive to all the antibiotics tested. Of 11 doctors tested 4 carried *Staph. pyogenes*: 2 of the strains were resistant to penicillin only, and 2 to penicillin and tetracycline. The group consisting of domestics, porters, and the staff of special departments, whose contact with patients was slight, is of interest in that most of the strains isolated were sensitive to all the antibiotics tested.

Effect of Closure of Ward and Spraying with Cetrimide

Those patients well enough to go home were discharged, 2 patients still infected with the epidemic strain were transferred to a fever hospital, and the 9 remaining patients, after their nose, skin, and bedding had been shown to be free from the infecting staphylococcus, were sent to other wards of the hospital. The whole ward, including side-rooms and corridor, was then thoroughly sprayed with cetrimide.

Air-dust samples.—In the next four days the air of the ward was sampled by exposing petri dishes containing nutrient agar plus phenolphthalein phosphate for two and a half hours. Swabs were also taken from the dust on the floor and plated out on a similar medium. In the main ward 49 plates were exposed and 24 dust swabs examined. Of the 73 plates thus used penicillin 10 units per ml. was added to the medium in 23, erythromycin in 26, and no antibiotic in 24. No colonies of *Staph. pyogenes* were isolated from any of these plates.

Similar tests were made in the side-rooms and the adjoining corridor; these consisted of three side-wards, kitchen, bathroom, sluice, linen-room, office, and laboratory. In each room 2–4 plates were exposed and 2 dust swabs were taken; in the corridor 5 plates were exposed and 3 dust swabs taken. In all, 49 plates were used: 18 contained penicillin, 19 erythromycin, and 12 no antibiotic. No *Staph. pyogenes* was isolated from the dust swabs, but 2 of the exposed plates yielded coagulase-positive staphylococci. One of these, containing penicillin, had been exposed in the linen-room and yielded two colonies; the other, containing erythromycin, had been exposed in the corridor just outside the linen-room and yielded one colony. All three colonies were of the epidemic type.

In view of the negative results obtained everywhere except in the linen-room, in spite of the rather searching tests in which large numbers of plates had been exposed for two and a half hours, it was decided to fumigate the linen-room without retreatment of the rest of the ward. Twenty-four hours after this had been done, 9 plates without antibiotic were exposed for two and a half hours in the linen-room and the adjoining corridor. Four colonies of *Staph. pyogenes* were isolated from 1 plate exposed in the corridor. Since none of these was resistant to any other antibiotic than penicillin, it was decided to reopen the ward.

Bedding.—The beds were all made up with linen and blankets treated with arquad, and similarly treated curtains were supplied. Sweep-plates were taken from two blankets and one curtain of each bed before the admission of patients. *Staph. pyogenes* was isolated from one blanket and one curtain. In each case only a single colony was found; that from the blanket was sensitive to all the antibiotics tested, and that from the curtain was resistant to penicillin only.

Discussion

In each of these outbreaks a single strain of *Staph. pyogenes* resistant to penicillin, tetracycline, and erythromycin was widespread in the ward environment, and in each case there is evidence that the strain was introduced into the ward by a patient with superficial skin sepsis. Although the epidemic strain was isolated from the sister in the surgical ward, more probably she was a reflection of the epidemic than its cause, since strains of *Staph. pyogenes* resistant to erythromycin had not been found in this ward before the admission of case 1 and were very uncommon elsewhere in the hospital. None such had been found when nasal swabs from 540 nurses were examined ten weeks previously.

The outbreak in the medical ward was associated with no severe sepsis, and the strain was apparently eradicated by removing the infected patient, treating the nasal carriers, and changing all the blankets for those treated with a quaternary ammonium compound. In the surgical ward, however, there were 11 cases of infection, many of them severe, and the strain was eliminated only after closure of the ward and spraying with cetrimide.

Probably both the host and the parasite played a part in this difference. As regards the host, patients after operations are highly susceptible to infection. McDermott (1956) has suggested that an " increased congregation of more susceptible hosts " is one of the main reasons for the apparent increase in staphylococcal infections in hospitals today.

The virulence of the invading staphylococcus must not, however, be overlooked. *Staph. pyogenes* of phage type 80, the type responsible for the outbreak in the surgical ward, was first isolated in 1953 by Rountree and Freeman (1955) in Australia. They regarded the strain as a new phage type of *Staph. pyogenes* of " enhanced virulence ", because of the severity of the lesions and the predominance of this strain in outbreaks of neonatal infection in 1954 throughout Australia. Since then other workers have reported outbreaks of unusually severe staphylococcal infection due to strains of this type in Great Britain (Anderson and Williams 1956, Gillespie and Alder 1957, Duthie 1957).

It cannot be assumed from this that strains of certain phage types are necessarily more virulent than those of other types. Probably the virulence of most strains of *Staph. pyogenes* may become enhanced in infections (Barber and Burston 1955) and by passage through patients (Rountree and Freeman 1955, Beaven and Burry 1956).

Antibiotic Sensitivity of Infecting Strains

In the surgical ward the infecting strain was initially erythromycin-sensitive but yielded an erythromycin-resistant variant during the treatment of 1 patient with this antibiotic for seven days. Such occurrences are well known with erythromycin (Wise et al. 1955, Thomson et al. 1956); and Hobson (1954) and Garrod and Waterworth (1956) have shown that staphylococci produce strains resistant to erythromycin more readily than they produce strains resistant to any other antibiotic except streptomycin.

In both wards an occasional variant resistant to chloramphenicol was found. This finding is unexplained, and there is no known correlation between resistance to erythromycin and resistance to chloramphenicol. Since both the infecting strains were resistant to several antibiotics, it is possible that they were highly mutagenic. Chadduck et al. (1954), working with *Escherichia coli* K.12, have shown that certain strains of this species have mutator genes, which give them an increased rate of mutation to drug resistance and other characteristics. The same may be true of staphylococci.

Preventive Measures

As long as septic cases are admitted to general wards, hospital cross-infection will continue. The present study shows the importance of superficial skin infections in this respect and confirms the observation of Barber and Bursten (1955) that nasal carriers may be relatively unimportant. In both wards numerous strains of *Staph. pyogenes* were present in the environment, but a newly introduced strain spread round the ward to a much greater degree than any of the strains previously present. It is improbable that all strains of *Staph. pyogenes* could be excluded from a ward; but, if we really face the fact that staphylococcal sepsis is a communicable disease, there is nothing to prevent hospitals from having isolation blocks to deal with this problem.

Meanwhile something, no doubt, can be done by barrier nursing and by treating the bedding. The difficulty of applying the former adequately in a busy general ward is, however, extreme. The danger of blankets as a source of infection can be reduced. Barnard (1952) showed that they were not only sterilised by impregnation with estyl pyridinium bromide (' Fixanol C ') but also remained, to some extent, self-disinfecting. Blowers and Wallace (1955) and Frisby (1957) recommended washing the blankets in a non-ionic detergent (' Lissapol ') and then soaking with a cationic detergent (' Currasol '). In the present study arquad was the quaternary ammonium compound used.

Finally the whole hospital policy in relation to staphylococci needs reviewing. It would almost certainly be impossible and not necessarily desirable to eliminate the whole genus from the hospital environment. It might be more sensible and would certainly be more practicable to select relatively harmless strains. There is much evidence that pathogenic and non-pathogenic staphylococci are variants of a single species, and that white, golden, or even lemon-yellow strains may, under certain rare conditions, arise one from another (Hoffstadt and Youmans 1932, Pinner and Voldrick 1932, Barber 1955). Certainly strains of staphylococci may show all permutations or combinations in relation to the production of pigment and of alpha-lysin, coagulase, and other toxic substances (Barber et al. 1953).

The haphazard and wholesale use of antibiotics in hospitals in the last fifteen years has selected strains of staphylococci which are not only resistant to many of these powerful weapons but also, possibly because they have been freed from competition with lesser breeds, liable to give rise to strains of enhanced virulence (Howe 1954, Beaven and Burry 1956, Barber 1958). A hospital antibiotic policy designed to reverse this process, in association with the exclusion of multiple-resistant strains from the general wards, might have far-reaching results. It may well be that the best approach to the problem of staphylococcal cross-infection is to learn how to select staphylococci of lower infectivity and virulence and to render human beings more resistant to their toxic products. In the New Jerusalem, when the lion lies down with the lamb, is it too much to hope that man will have learnt to live at peace with the staphylococcus?

Summary

Staphylococcal outbreaks in a medical ward and a surgical ward are described. Each was due to the admission of a patient with superficial staphylococcal infection.

In both outbreaks the offending staphylococcus was resistant to erythromycin as well as to penicillin, streptomycin, and tetracycline, and in one outbreak the erythromycin resistance followed treatment of the initial patient with this antibiotic.

In the medical ward, although the bedding of 7 patients, in widely scattered areas of the ward, was infected, there were no cases of severe sepsis. After the infected patients had been discharged and all the blankets and ward curtains had been superseded by fabrics treated with a quaternary ammonium compound, the epidemic strain was no longer found.

In the surgical ward a single strain of *Staph. pyogenes* of phage type 80 caused severe infections (of which one was fatal) in 8 patients, 2 nurses, and 1 surgeon. The offending strain was only eliminated by closing the ward and by spraying with cetrimide.

It is a pleasure to thank the many colleagues, especially Nurse H. M. Higham, who not only made this investigation possible but also assisted us in every way, and Dr. R. E. O. Williams and Dr. Patricia Jevens, of the Central Public Health Laboratory, Colindale, for phage typing many of the strains and supplying us with bacteriophages so that we could continue for ourselves.

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TONGUE BIOPSY

A TECHNIQUE USING A RIGID SUCTION TUBE

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THERE have been many excellent reports of the macroscopic appearance of the tongue in disease (Sircus et al. 1957), particularly of its value as an indication of deficiency of riboflavine, nicotinic acid, and protein (Spies et al. 1938). In pernicious anæmia, the appearance of the tongue improves after the administration of cyanocobalamin vitamin B^{12} (Brown 1949).

In Australia Bolton and his colleagues have made valuable studies of the appearance of the tongue in malnutrition and pregnancy (Bolton 1958, Bolton and Forster 1958) and have correlated the changes with the neurological findings (Bolton 1955) and the level of serum-albumin (Gandevia and Hossack 1955).

A survey of the recent literature available to us has revealed no such studies based on biopsies of the epithelium of the tongue, though tongue biopsy has been used to investigate local lesions such as cancer.

Our purpose here is to describe our experience with tongue biopsy, with special reference to a new biopsy tube designed in our unit. It is a modification of the flexible suction gastric biopsy tube first described by two of us (Wood et al. 1949).

Only a limited report can be given of the histological findings: a full discussion will be published when further data become available, especially concerning serial biopsies in 1 patient.

The study was begun by using fine scissors to cut small fragments of epithelium, but this proved unsatisfactory, especially when the central zone was being examined. It was difficult to obtain sufficient depth without causing the patient subsequent discomfort by exposing too great an area. After 17 biopsies had been cut with fine scissors with only moderate success it became apparent that a suction biopsy tube would be preferable, because it would remove a full depth of epithelium and some underlying substantia propria from a limited area. Following a number of trials a rigid suction tube was designed which produced suitable fragments.

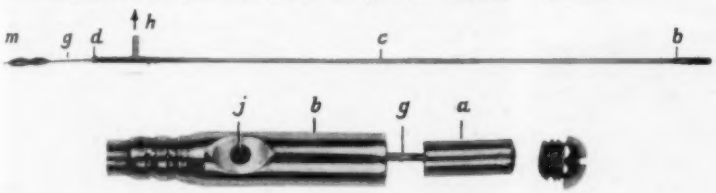


Fig. 1—Rigid suction-tube for tongue biopsy, with details of operating head.

The Tube

The tube † (fig. 1) consists of a cylindrical knife (a) and head (b) about 3 cm. long and 6 mm. outside diameter rigidly mounted on one end of a stainless-steel tube (c) 41 cm. long and 4 mm. in diameter. The proximal end is fitted with a suction-tight gland (d) and a lateral tube (h) through which suction is applied. The knife (a) 11 mm. long and 4 mm. diameter has a proximal cutting edge and is screwed on to the end of a 19-gauge spring steel wire (g), which traverses the length of the tube and emerges through the gland at the proximal end where it is fitted with a detachable handle (m). A hole (j), 2 mm. in diameter, countersunk to a maximum diameter of 7 mm., is drilled laterally in the wall of the head (b). A terminal screw seals the end of the head, and when unscrewed allows the knife to be detached. The outside wall of the head, diametrically opposite the hole, is marked to permit accurate location of the hole on the tongue. On operation a suction of 40 cm. Hg. is applied; a small fragment of tongue is sucked into the hole (j) and is cut off when the knife is operated.

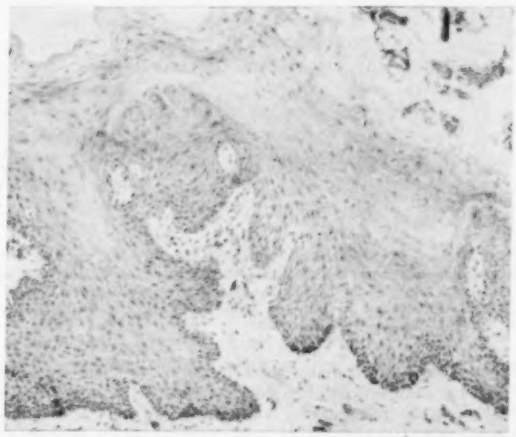


Fig. 2—Biopsy of normal tongue. Actively proliferating basal cells lie between primary and secondary papillæ in substantia propria; prickle cells are numerous; superficial squamous cells have formed filiform papillæ, and groups of cocci are visible on desquamating cells in upper right-hand corner. (Hæmatoxylin and eosin. × 150.)

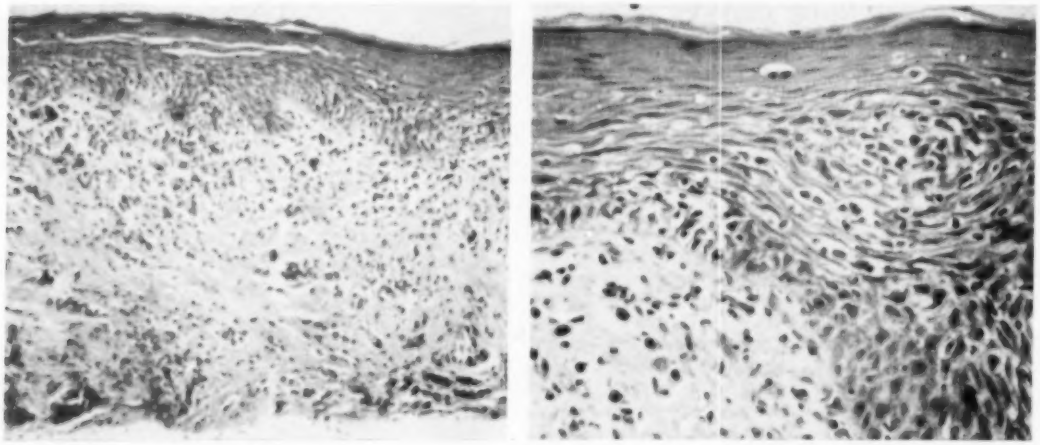
Technique

The patient lies with his head supported by a pillow. The operator sits on his left and grasps the tip of the protruded tongue after wrapping it in gauze. The area selected is swabbed with benzalkonium chloride and alcohol, and then 3% cocaine in 1 : 10,000 adrenaline. A fine needle (26 gauge) is inserted at an angle of about 30° and 0·3 ml. of procaine 2% solution is slowly injected below the epithelium.

The biopsy tube is applied lightly and accurately over the area of anæsthesia, the position of the lateral hole being indicated by the location mark on the instrument. The proximal end of the tube is held by an assistant, who depresses the operating handle to open the lateral hole, applies negative pressure to suck in the fragment, and immediately pulls up the knife blade. This operation may be repeated over a neighbouring site to obtain a second fragment. The fragment is retrieved by removing the terminal screw and unscrewing the cylindrical blade. A fragment remaining in the cylinder may be blown out by a stream of air.

* Working with the aid of a grant from the National Health and Medical Research Council of Australia.

† This biopsy tube is made by H. A. Taylor and Son (Surgical) Pty. Ltd., 44, Macfarlan Street, South Yarra, Melbourne, Victoria, Australia.



(A) (B)

Fig. 3—Tongue biopsy in atrophic glossitis. Woman, aged 45, with chronic hepatitis, malnutrition and recurrent glossitis. Tongue was painful, ulcerated, red, and smooth. A, gross thinning of epithelium and loss of filiform papillæ, while primary and secondary papillæ have disappeared; heavy inflammatory infiltration of substantia propria and epithelium. (Hæmatoxylin and eosin. × 300.) B, thin basal and prickle-cell layers of epithelium, and infiltration of substantia propria and penetration of epithelium by lymphocytes. (Hæmatoxylin and eosin. × 600.)

The fragment is immediately fixed in 10% formol saline and when embedded in paraffin, oriented to obtain a vertical section of the mucosa.

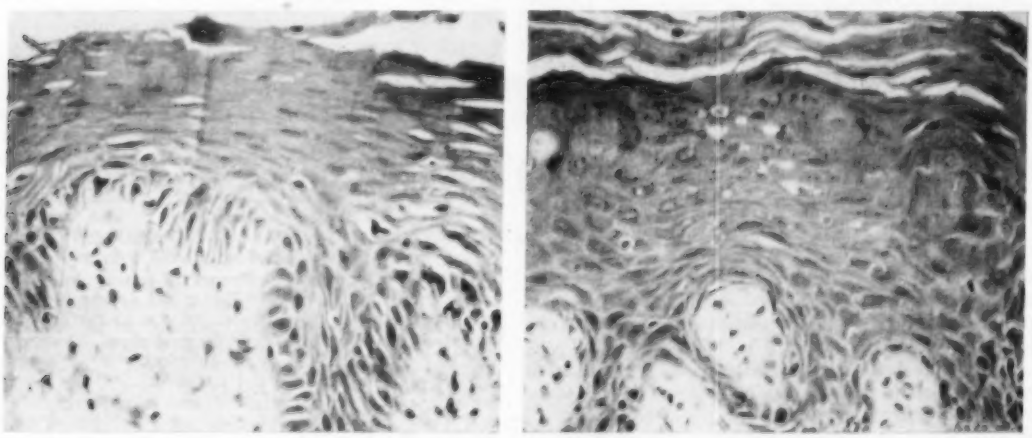
Results

With this model 50 successful biopsies have now been made at 53 attempts on 40 people whose tongues either appeared normal (17) or showed atrophy or inflammation (33). The specimen was usually taken from an area about 2 cm. from the tip and mid-way between the median groove and the lateral edge. On 18 occasions two fragments were obtained from neighbouring sites. 6 people had further biopsies a week or more later, 1 having 4 biopsies, 2 having 3, and 3 having 2. The 3 failures were all in people with considerable atrophy of the epithelium—1 with pernicious anæmia, 1 with recurrent glossitis, and 1 with malnutrition and atrophic glossitis. In 2 of these, small fragments were subsequently obtained by fine scissors, but this was difficult and caused relapse in the case of ulcerative glossitis.

In the 50 successful biopsies when the suction tube was used, no major discomfort was felt either during or after the operation. Most subjects reported no discomfort; a few had slight soreness of the tongue for twenty-four hours.

Pathology of Biopsy Fragments

Biopsies of the anterior upper surface of the normal tongue presented an appearance in keeping with standard descriptions (Maximow and Bloom 1948), the three layers (superficial squamous, prickle, and basal) being clearly identified. Certain regions showed evidence of more rapid proliferation of the basal cells, these cells forming a layer three to six cells thick and being cuboidal



(A) (B)

Fig. 4—Tongue biopsy, showing glossal atrophy. Woman, aged 51, with untreated pernicious anæmia. Tongue was red, smooth and atrophic. A, considerable thinning of epithelium. Basal layer is only one or two cells in depth and few prickle cells remain. There is thin smooth superficial squamous-cell layer. (Hæmatoxylin and eosin. × 600.) B, after treatment with vitamin B_{12} for six weeks. Basal-cell proliferation is more pronounced; numerous prickle cells are present. Keratohyaline granules are visible in superficial squamous-cell layer. (Hæmatoxylin and eosin. × 600.)

or low columnar in shape, with darkly staining oval nuclei and scanty cytoplasm (fig. 2). More superficially the cells were prickle-cell in type, forming a layer about six cells thick. Here the cells were oval or spindle-shaped, with paler staining and irregularly shaped nuclei, and peripheral intercellular bridges visible under higher magnification. More superficially again there was a squamous-cell layer, often containing keratohyaline granules. At the surface these cells formed filiform papillæ, whose surface was roughened by desquamating cells which often contained groups of cocci (fig. 2). Biopsy on " furred " tongues showed excess amounts of this superficial cellular material and cocci. Over fungiform papillæ the surface was smooth.

In regions where basal-cell proliferation appeared less active, the basal-cell and prickle-cell layers were only one or two cells in depth, while the squamous layer was thin and smooth. Under these areas the substantia propria projected up to form primary and secondary connective tissue papillæ. These normally contained some thin-walled capillaries and an occasional fibroblast and mononuclear cell (fig. 2).

When there was macroscopic glossal atrophy good general correlation was found with the histological appearances. Here the areas of slower basal-cell proliferation were increased and tended to coalesce, with a corresponding reduction or disappearance of the regions of rapidly multiplying basal cells (fig. 3). This produced a thin smooth mucosa in which filiform papillæ had disappeared: all three layers of the stratified squamous epithelium were reduced in width and the primary and secondary connective-tissue papillæ were absent.

Biopsy of a tongue showing moderate macroscopic atrophy revealed loss of the filiform papillæ and decrease in prickle cells; with gross macroscopic atrophy there was thinning of all epithelial layers and absence of the papillæ of the substantia propria.

With atrophy of the epithelium the coccal colonies disappeared, possibly because of a decrease in the supply of nutritional factors afforded by the normally desquamating cells. Such a decrease in the normal bacterial flora and a reduction of the mechanical barrier may predispose the tongue to bacterial infection and inflammation.

In a case of pernicious anæmia with considerable atrophy of the epithelium, the biopsy was repeated after six weeks of treatment with vitamin B_{12} (fig. 4). Even allowing for slight variation in the cutting angle of the sections, there was an increase in the thickness of the basal and prickle-cell layers, and keratohyaline granules had formed in the squamous layer. The connective-tissue papillæ were also increased in depth.

The only inflammatory changes observed in this series were an increase in the lymphocytes, plasma cells, and mononuclear cells in the substantia propria. Lymphocytes were frequently seen penetrating the epithelium, lying in small vacuoles between the cells (fig. 3).

Discussion

In this limited experience there was good correlation between the appearance of atrophy of the tongue and the biopsy findings. When the tongue appeared normal, the biopsy revealed stratified squamous epithelium which could be seen as a plate of proliferating basal cells. In some areas proliferation appeared to be more rapid than in others, producing an uneven epithelial layer. With the development of atrophy the basal-cell proliferation became slower and more even, thus producing a thin smooth epithelium.

In 1 case of pernicious anæmia the administration of vitamin B_{12} was followed by a cellular response towards a more normal epithelium—a change parallel to that seen in other proliferating cells such as the hæmopoietic bone marrow, but absent in the gastric mucosa (Doig and Wood 1950, Finckh and Wood 1953).

It may well be that studies based on biopsy of the tongue will throw further light on the degenerative processes in various diseases, especially with regard to the cellular changes. Serial biopsies on a single patient may also produce critical evidence of the value of various therapeutic measures.

Summary

A rigid suction tongue-biopsy tube is described.

50 successful biopsies were made in 40 people whose tongues either appeared normal or showed atrophy or inflammation. There was no major discomfort either at operation or later.

The fragments obtained were suitable for histological examination. There was a full depth of epithelium with some underlying substantia propria. When the tongue appeared atrophic there was good correlation between macroscopic and histological appearances.

Studies based on biopsy of the tongue may throw further light on the degenerative processes in various diseases, especially with regard to the cellular and tissue changes. Serial biopsies may aid in assessing the value of treatment.

Our thanks are due to the members of the honorary medical staff of the Royal Melbourne Hospital for sending patients for examination; to Miss E. Earle for skilfully preparing the histological specimens; and to Mr. R. Inglis, photographer to the Royal Melbourne Hospital, for providing fig. 1.

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COMPOSITION OF PLASMA CHOLESTEROL ESTER

IN RELATION TO CORONARY-ARTERY DISEASE AND DIETARY FAT

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THE fatty acids of cholesterol esters (C.E.F.A.) in plasma are highly unsaturated (Bloor et al. 1938, Kelsey and Longenecker 1941, Michalec 1956), the mean iodine value (I.V.) in man being 157·8 in Bloor's series. Prominent among the unsaturated C.E.F.A. are linoleic and (to a lesser extent) arachidonic and linolenic acids, which are essential in that they cannot be synthesised in the mammalian body from saturated fats or acetate and that pathological changes take place in some animals fed on diets deficient in them. Many vegetable oils containing a preponderance of these fatty acids have the property of lowering the serum-cholesterol (Ahrens et al. 1955), Frishley et al. 1955, Bronte-Stewart et al. (1956), appar-

FATTY ACIDS OF CHOLESTEROL ESTER OF PLASMA IN NORMAL BANTU AND WHITE SUBJECTS, AND IN PATIENTS WITH CORONARY-ARTERY DISEASE (EXPRESSED AS MEAN AND STANDARD DEVIATION)

—	Bantu	White	Coronary-artery disease
Ester cholesterol (mg. per 100 ml.)	91 (32)	141 (12)	151 (31·5)
Iodine value	179 (26·5)	160 (34·5)	136 (35·6)
% Linoleic	55·4 (10·8)	53·2 (10·7)	40·6 (15·5)
% Linolenic	8·6 (4·3)	5·1 (2·5)	5·4 (2·8)
% Arachidonic	13·6 (4·9)	9·5 (2·3)	7·6 (3·0)
% Pentaenoic	1·2 (0·8)	1·4 (0·5)	2·1 (1·0)
% Hexaenoic	3·2 (2·0)	2·5 (2·7)	2·8 (2·7)
% Saturated + oleic	18·0	28·3	41·5

ently by accelerating the catabolism of this sterol to bile acid (Lewis 1957, 1958).

Studies on *total* serum fatty acids have been reported from several centres. Wiese et al. (1956) have found that trilinolein feeding increases the percentage of linoleic and arachidonic acids. Hammond and Lundberg (1955), comparing Guatemalans on low fat intakes, atherosclerotic subjects, and blood-bank donors, demonstrated lower percentages of linoleic and arachidonic acids, but a probable higher percentage of linolenic acid, in the atherosclerotic group. Also employing the technique of alkali isomerisation for the analysis of polyunsaturated fatty acids, Antonis (1957) reported a lower percentage of linoleic acid in atherosclerotic patients than in normal white subjects, while Bantu mine labourers had far higher percentages of linoleic and arachidonic acids. On the other hand, James et al. (1957) were unable to demonstrate an abnormality of serum fatty acids in patients with coronary-artery disease, using vapous phase chromatography as the analytical procedure. In interpreting these studies it should be noted that total serum fatty acids may not represent a homogeneous physiological entity.

These interrelationships suggested an investigation into plasma C.E.F.A. composition in coronary-artery disease, and as a corollary, in Bantu subjects, whose susceptibility to this condition is exceedingly low.* Feeding experiments have been carried out to ascertain whether plasma C.E.F.A. were affected by the nature of the dietary fat. C.E.F.A. from atheromatous coronary arteries have also been analysed.

Twelve white patients who had had one or more cardiac infarctions were studied. They were ambulant, and were selected in that their dietary habits (so far as could be ascertained) had not been changed after their illness; at the time of the survey none was receiving anticoagulant therapy. Twelve Bantu subjects were investigated: they were clinically normal, and care was taken to exclude any whose dietary and other customs might have been modified by urbanisation. Eight white subjects, clinically and electrocardiographically normal, served as controls. The samples were analysed without prior knowledge of the group to which they belonged. The mean ages of the three groups were 40, 35·5, and 48 years respectively.

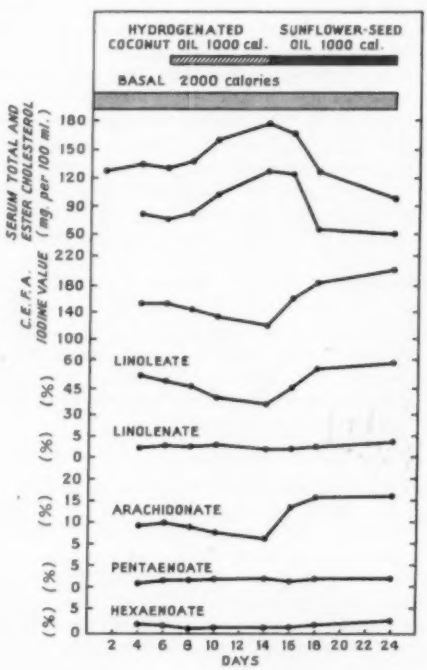
Plasma was extracted within one hour of venesection, using ten volumes of methylal-methanol 4:1 (Delsal 1944). The total lipid was fractionated according to the procedure of Fillerup and Mead (1953) by chromatography on silica gel, previously deactivated and washed with methanol and ether containing 0·1% hydroquinone to remove adsorbed oxygen, and finally washed with petroleum ether. Saponification of cholesterol esters was carried out at 35°C using potassium *tert*-butoxide; cholesterol was removed, the soaps were hydrolysed, and the fatty acids extracted conventionally. Fatty acids were determined by electrometric titration to pH 9·0 with 0·01N ethanolic potassium hydroxide, assuming a mean molecular weight of 286. A micro-bromine addition procedure (Trappe 1938) provided a measure of overall unsaturation, and poly-unsaturated fatty acids were characterised and determined by the alkali isomerisation technique of Herb and Riemenschneider (1953); saturated plus oleic acids were computed by difference. All operations were performed in a nitrogen atmosphere.

As the table shows, C.E.F.A. iodine values were highest in the Bantu group and lowest in the patients with coronary-artery disease. This was due mainly to differences in linoleic and in arachidonic acid percentages, and reciprocally in saturated (mainly palmitic by paper chromatography) plus oleic acids. The coronary group had the highest and the Bantu the lowest total lipid levels.

Application of the t test showed that the differences between the C.E.F.A. iodine values of the three groups were significant at the 5% level, that between the Bantu and coronary groups being almost significant at the 1% level. The differences between the percentages of arachidonic acid were also significant at the 5% level, but linoleic acid differed significantly only between white and coronary and between Bantu and coronary groups.

Feeding experiments were carried out on two normal Bantu subjects in the metabolic ward. The basal diet contained 5 g. of fat. Dietary oils were substituted isocalorically for carbohydrate. Administration of hydrogenated coconut oil (I.V. 6) and sunflower-seed oil (I.V. 135) was shown to produce wide variations in C.E.F.A. unsaturation. In the experiment shown in the chart, the C.E.F.A. iodine value fell to 122 during coconut-oil feeding and rose to 199 when this was replaced by sunflower-seed oil. Linoleic and arachidonic acids were the most labile. Administration of the latter oil elevated the percentage of these acids in C.E.F.A. before the serum-cholesterol fell significantly.

Atheromatous coronary arteries were found to contain relatively saturated C.E.F.A. Using similar analytical techniques, a mean I.V. of 64 was obtained in material



* Several other biochemical, hæmatological and clinical modalities were investigated by Dr. C. Merksey, Dr. H. Gordon, Dr. R. Lackner, and Dr. H. Nossel. These will be published separately.

from four autopsies; 81% of the C.E.F.A. comprised saturated and oleic acids, the percentages of acids with two, three, four, five, and six double bonds being 11, 3·3, 3·6, 0·31, and 0·43 respectively. This finding agrees with the observations of Schönheimer (1926) and Keegan and Gould (1953), who found the predominant fatty acids in human aortic plaques to be stearic, palmitic, and oleic. There is a possible parallel to this example of a higher degree of saturation of tissue-C.E.F.A. in comparison to circulating esters: Alfin-Slater et al. (1954), working on rats, have found that deficiency of essential fatty acids leads to deposition of cholesterol and fat in the liver. Achaya et al., cited by Deuel (1955), have shown further that under these conditions liver-cholesterol, normally esterified to a large extent with oleic acid, becomes bound to saturated acids.

Using the data obtained in the survey, regression equations were calculated for plasma ester-cholesterol against C.E.F.A. iodine value, and against the percentages of linoleic, arachidonic, and palmitic plus oleic acids in plasma C.E.F.A. The correlation coefficients for the same data were all significant at the 5% level by Fisher's z test. This corresponds to the observation, in the feeding experiments, of a reciprocal relation between plasma ester cholesterol and the content of certain unsaturated fatty acids in plasma cholesterol esters.

The regression lines for these sets of variables were somewhat dissimilar in the three groups studied, but the differences in slope were not statistically significant.

Thus the proportion of saturated and oleic acids in the C.E.F.A. was far higher in atheromatous plaques than in plasma, while in plasma itself it was highest in subjects with established coronary-artery disease and lowest in the Bantu. In the light of these studies it seems possible that a primary effect of dietary unsaturated fats is to increase the unsaturation of circulating cholesterol esters, perhaps rendering their solution in plasma more stable or making the cholesterol more susceptible to catabolism to bile acid. However, the high concentration and probable functional importance of poly-unsaturated fatty acids in intracellular organelles (Kretchmer and Barnum 1951) have also to be considered. Feeding a diet rich in such acids may conceivably facilitate certain metabolic activities, including cholesterol catabolism.

This study was carried out as part of the programme of the Clinical Nutrition Research Unit supported in the University of Cape Town by the South African Council for Scientific and Industrial Research. It is a pleasure to acknowledge my indebtedness to Dr. H. Gordon for his invaluable assistance in selecting the clinical material for the survey, to Prof. J. F. Brock and Dr. C. Merskey for their encouragement, and to Mrs. L. Rose-Innes for technical assistance.

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CHRONIC DISSECTING ANEURYSM OF THE AORTA DIAGNOSED BY AORTOGRAPHY

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DISSECTING aneurysms of the aorta usually run a rapid clinical course and are often fatal within twenty-four hours. Shennan (1934) examined 143 recent dissecting aneurysms and found that 84% of the patients died within the first week. However, it is now well recognised that patients occasionally recover from the initial episode and may live for many years with the condition unrecognised. According to Drury (1955), who reported 2 such cases, most of the healed aneurysms described fell into a surprisingly uniform pattern. Most are "double-barrelled aortas" extending from the distal part of the arch of the aorta to the bifurcation. They show clear evidence of patency, and their sacs become lined with endothelium and may contain varying degrees of atheromatous change.

It is difficult to assess the real frequency of healed aneurysms of the aorta. Weiss et al. (1940) estimate that one dissecting aneurysm in ten is apt to heal.

It is clear from the literature that a correct diagnosis of chronic dissecting aneurysm is rarely made during life. Even less commonly is positive proof of the diagnosis obtained before necropsy. For these reasons the following case is considered worthy of recording.

Case-report

On Oct. 8, 1952, a painter, aged 43, was seized with a severe pain in the chest and back while drinking a cup of tea. The pain was continuous but was worse with breathing. He remembered having a similar pain twenty years before, after an accident. On admission to University College Hospital, he was pale, and in obvious pain, but was not shocked. The blood-pressure was 130/80 min. Hg, but rose within a few hours to 210/130 and thereafter remained at about this level. The pain gradually lessened, and after a week, with a morning pyrexia, the patient seemed fairly well again. An electrocardiogram on admission and another next day proved normal.

Blood-culture during the first twenty-four hours grew a non-hæmolytic streptococcus. A leucocyte-count of 14,000, with 82% polymorphs, was found on admission. The diagnoses considered were small dissecting aneurysm, spontaneous perforation of the œsophagus, and Bornholm disease. Several radiographs of the chest, taken after admission, showed a slight increase in the breadth of the mediastinum, which was thought to be significant. A clinical diagnosis of dissecting aneurysm was made. His recovery was uneventful, and he was discharged perfectly fit four weeks after admission, but without a firm diagnosis.

He returned home and to his work, and remained well until the following year when he collapsed and was admitted to Hillingdon Hospital. Shortly afterwards he had a large hæmatemesis. He was treated medically and recovered well. Duodenal ulceration was diagnosed after a barium-meal examination. He remained well on an ulcer regime until 1956.

During 1956 he developed a bloated feeling in the abdomen, and was found to have a pulsatile abdominal swelling which was thought by Mr. J. R. Elder to be an aortic aneurysm.

On admission to St. Mary's Hospital on June 26, 1956, he appeared to be in fairly good health. The pulsatile abdominal swelling could easily be felt below and to the left of the umbilicus. The blood-pressure was 220/120, and the apex beat was displaced to the left. No hypertensive changes were noted in

the fundi, and the urine contained no albumin. The blood-urea was 36 mg. per 100 ml. On June 29, lumbar aortography was performed by Dr. D. F. Reynolds of the radiological department, to define the exact site and size of the suspected aneurysm, and showed the rather unusual appearances illustrated in fig. 1. These gave rise to some controversy but were finally attributed to a dissecting aneurysm. It was thought that the needle point had entered the sac of the aneurysm which was clearly visualised, and that the contrast medium was then entering the true lumen of the aorta, which was also shown, though less clearly, on the serial films. It was suggested that the diagnosis could be confirmed and the true lumen of the aorta adequately shown by retrograde catheterisation from the femoral artery, and this was done by one of us (D. S.) on July 25. The aorta was readily catheterised, and contrast injections showed the appearances illustrated in fig. 2. These confirm that the true lumen of the aorta was separate from the lumen of the dissecting aneurysm demonstrated by lumbar aortography and was somewhat compressed by it. They suggested that the dissecting aneurysm began somewhere in the region of the aortic arch and finished in the region of the common iliac arteries. They also suggested that the dissecting aneurysm was interfering with the blood-flow to the kidneys.

Fig. 1—Lumbar aortogram. The needle has entered the sac of a dissecting aneurysm, which is shown extending up into the thorax. Contrast medium has passed from the aneurysm into the true lumen of the aorta, which is shown lying parallel to the dissecting aneurysm and to its left.

This interesting finding raised the possibility that the hypertension might have been caused by the encroachment of the dissecting process upon the lumen of one or both the renal arteries. Further investigation of the renal function showed that both kidneys seemed to function adequately. It was thought, however, that if his blood-pressure could be reduced it would improve the long-term prognosis, and hypotensive therapy was therefore instituted.

When seen in December, 1957, the patient remained well and free from fresh symptoms.

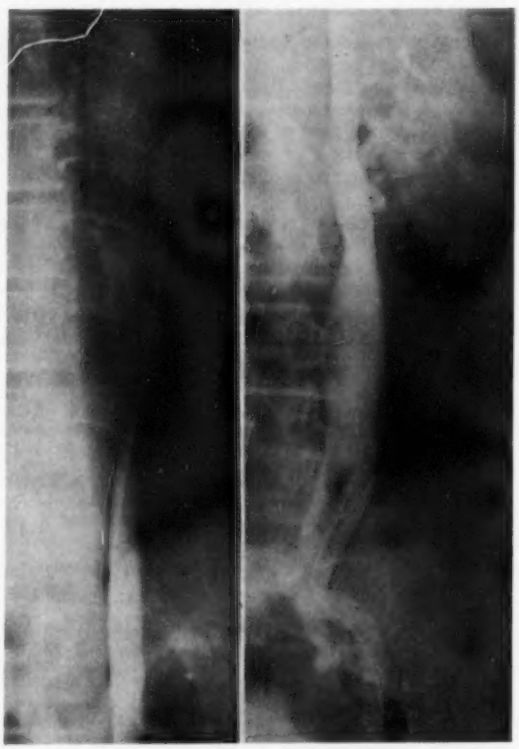
Discussion

The diagnosis of dissecting aneurysm, rarely made during life, may be suggested on a plain radiograph by progressive enlargement of the aortic shadow on serial films of the chest. This possibility was raised in our patient on his original admission at University College Hospital. However, this is a sign that must be treated with caution and can be misleading. Great care must be taken that the serial films are exactly comparable. One of us has seen a case where the diagnosis was confidently suggested on plain X-ray grounds, but not confirmed at necropsy. The apparent mediastinal increase in width was then presumed to be largely artefact.

The use of contrast media will allow positive proof of the diagnosis, but few previous cases can be found where these have been used. In a case reported by Halliday (1952), a dissecting aneurysm was demonstrated by angiocardiography in the acute stage. In another case of acute dissecting aneurysm (Warren et al. 1956) a positive diagnosis was obtained by an aortic catheterisation in November, 1956.

In our case a positive and unequivocal diagnosis was made by contrast vascular studies: not only was the aneurysm itself directly demonstrated by lumbar aortography, but the original lumen of the aorta was clearly visualised by percutaneous catheterisation from the femoral artery.

The angiographic findings in this case support the opinion of Drury (1955), who held that most of the patients who survive are those with a normal ascending aorta, and that most healed dissecting aneurysms begin at or near the aortic arch. He was also of the opinion that the second factor that appeared to encourage healing was the length of the aneurysm. Shennan's (1934) series was quoted to support the view that short dissections rupture early, and most healed dissecting aneurysms are long and sheath-like, extending from the arch to the iliac arteries. He explains this by the hypothesis that the pressure within the aneurysm will equal that of the thoracic aorta at the point of primary tear from which it arises. On the other hand, the pressure within the aorta will be lowered distally by successive branching. A re-entrant tear will then be favoured by the resulting pressure difference which increases with the length of the



(*a*) (*b*)

Fig. 2—Aortogram by femoral catheterisation. The true lumen of the aorta is demonstrated from the aortic arch down to the iliac arteries. The aorta is displaced to the left and compressed by the dissecting aneurysm (*a*), as are the common iliac arteries (*b*). There was faint filling of the dissecting aneurysm from the true aortic lumen.

Serial films show the lower limit of the dissecting aneurysm to lie in the right common iliac artery. The right renal artery was not demonstrated, and only a left nephrogram was obtained.

aneurysm. Local factors in the structure of the distal aorta and the iliac arteries may also be important.

Our case appears to support this concept. The primary tear is thought to lie in the region of the aortic arch and the re-entrant tear in the common iliac arteries.

Summary

A case of chronic dissecting aneurysm of the aorta complicated by hypertension is reported. The diagnosis was made during life by lumbar aortography and confirmed by transfemoral aortic catheterisation.

Our thanks are due to Prof. M. L. Rosenheim, of University College Hospital, for permission to use the case-notes concerning the patient's first hospital admission in 1952.

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HYPOKALÆMIA FOLLOWING CHRONIC DIARRHŒA FROM OVERUSE OF CASCARA AND A DEFICIENT DIET

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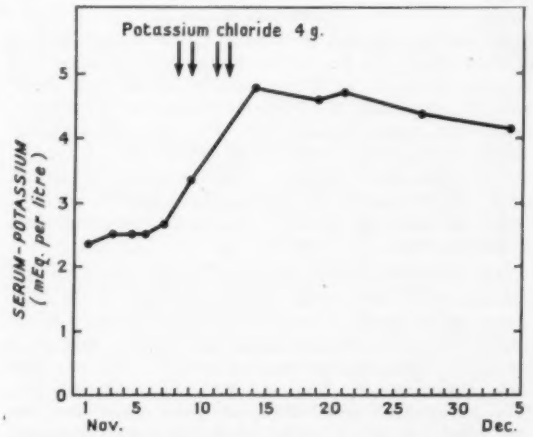
SEVERE potassium depletion and hypokalæmia following chronic diarrhœa induced by overuse of laxatives have been described in two otherwise healthy women by Schwartz and Relman (1953). In the case described here severe hypokalæmia developed in similar circumstances in a man aged 78. Associated muscular weakness of the limbs led to an initial diagnosis of cerebral thrombosis, but a routine electrocardiogram showed changes indicating hypokalæmia, which was confirmed biochemically.

Case-report

A man, aged 78, came into hospital on Oct. 27, 1956, because of sudden loss of power in his arms and left leg. On the previous evening he had fallen asleep in a cinema and wakened with weakness of his limbs. He made his way with difficulty to his lodging-house. His doctor noted weakness of both arms and the left leg and sent him into hospital next day with a provisional diagnosis of cerebral thrombosis.

On admission the patient still had marked weakness of his arms. Abduction of his right arm and flexion of his left wrist and fingers were particularly affected. His tendon-reflexes were depressed in the arms, particularly the left. Power in his legs seemed, by this time, normal for one of his age and build. Next day, with no other treatment than rest in bed and an ordinary diet, he recovered power in his arms, and his tendon-reflexes returned to normal. On Oct. 30, 1956, routine electrocardiography showed changes indicating hypokalæmia. The serum-potassium level was 2·3 mEq. per litre. The patient had not had any previous episodes of this kind, but he had had transient weakness of his fingers during the week before admission to hospital.

Further observation showed that he was a depressed lonely old man. He had retired from labouring nine years previously. He had left his native Ireland as a young man and had no relations, and few friends in Scotland. He felt unwanted and had the idea that the people in his lodging-house complained of an unpleasant smell emanating from him. He thought this was the result of food rotting inside his body, and that it could be corrected by frequent aperients. Consequently he had for months, if not years, taken two cascara tablets three times each day. He was secretive and evasive about his bowel movements, particularly after he was forbidden laxatives, and



Serum-potassium levels, showing effect of increased intake of potassium.

refused to cooperate in the collection of specimens. He regarded himself as constipated if he had fewer than three bowel movements in the day.

Diet.—He was vague about his dietary habits. He had bought and prepared his own food for years and seemed to have lived for a considerable time on a diet consisting largely of bread, margarine, and tea. He seldom, if ever, ate butcher's meat, bacon, or fish. He may have had up to three eggs in a week. He was 5 ft. 8 in. tall and weighed 7 st. 10 lb. when he came into hospital. He was thin but showed no overt sign of malnutrition.

Investigations.—His urine was acid. On repeated testing it was free from albumin, casts, and red cells and contained only an occasional leucocyte; it was sterile on culture on four occasions; its specific gravity was 1·008–1·012. The urinary excretion of potassium was 151·4 mg. in twenty-four hours on Nov. 7, 1956, and 72·8 mg. on Nov. 9. Potassium chloride 1 g. four times daily by mouth was given from Nov. 8 to Nov. 12, and the urinary excretion of potassium in twenty-four hours was 222·5 mg. on Nov. 10, 363 mg. on Nov. 14, and 685 mg. on Nov. 15. The serum-potassium level was initially 2·3 mEq. per litre and rose to the lower limit of normal after 5 g. of potassium chloride had been given and remained normal thereafter. The initial serum-bicarbonate level was 43·2 mEq. per litre and the initial serum-chloride level 84·0 mEq. per litre, but all the levels in the serum returned to normal and the electrocardiographic signs of hypokalæmia regressed as the serum-potassium level rose (see figure). On Nov. 27, 1956, the specific gravity of the urine after fourteen hours' deprivation of fluid was 1·012; two hours after the ingestion of 1 litre of water it was 1·002; corresponding figures on Dec. 6 were 1·018 and 1·001. Radiography of the chest, a barium meal, a barium enema, and intravenous pyelography showed no significant abnormality. Fat balance was attempted but had to be abandoned because the patient resented being forbidden purgatives. On Oct. 30, 1956 the erythrocyte-sedimentation rate was 14 mm. at the end of one hour (Westergren); the white cells numbered 8000 per c.mm.; Hb 11·9 g. per 100 ml. The Wassermann reaction of the blood was negative. The fasting blood-sugar level was 90 mg. per 100 ml. The levels of acid and alkaline phosphatase, calcium, and inorganic phosphate in the serum were normal.

Subsequent course.—The patient's general health improved gradually, and after he had been six weeks in hospital he had gained $1^1/_2$ stone in weight. Unfortunately, although his physical health was now quite satisfactory for a man of his years, his mental depression did not improve. He was admitted to a mental hospital in May, 1957. He died suddenly, apparently of coronary thrombosis, two months later. There was no necropsy.

Discussion

In health potassium is excreted by the kidney and, to a lesser extent, by the bowel. Depletion of potassium is usually the result of increased loss by one of these channels. In the present case the urinary content of potassium, when first measured, was low. The only abnormalities found in the urinary system were impairment of concentrating and diluting powers, which returned to normal after the potassium depletion had been treated. A renal defect of this kind is known to result from potassium depletion (Milne et al. 1957).

The bowel movements had been abnormally fluid and frequent for at least some months as a result of the daily ingestion of cascara. The serum-potassium level was not measured until a few days after the transient episode of paralysis. Probably the serum-potassium level was then even lower than the first, and lowest, recorded reading. The serum-potassium levels rose again slightly without any other treatment than the withholding of laxatives and the giving of an adequate diet. The administration of 5 g. of potassium chloride brought the serum-potassium level to the lower limit of normal. The total potassium supplement given was 16 g. of potassium chloride. Thereafter the serum-potassium level remained normal without any further potassium supplements. No abnormality was found in the gastrointestinal tract, and normal bowel function was restored when laxatives were discontinued. It is concluded that the potassium depletion and hypokalæmia with weakness of the limbs were due to increased fæcal excretion associated with a low intake of potassium.

Summary

A case of hypokalæmia with severe muscular weakness of the limbs is described.

The cause of the potassium depletion is thought to have been excessive use of cascara, causing chronic diarrhœa.

The dietary intake of potassium was low.

The hypokalæmia was diagnosed electrocardiographically.

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Preliminary Communication

AN ASSAY FOR INSULIN-LIKE ACTIVITY USING RAT ADIPOSE TISSUE

THE measurement of small amounts of insulin-like activity in blood and other biological fluids is still a problem. A specific and sufficiently sensitive chemical, chromatographic, or immunological method, while highly desirable, is not yet available. The assays so far developed are biological ones, based on insulin effects in vivo and in vitro—i.e., on induced hypoglycæmia in rats and mice sensitised by endocrine manipulations,[1–3] on measurement of glucose uptake by the isolated rat hemidiaphragm,[4–6] or gas formation by mammary gland of the lactating rat.[7] Because of the small maximal insulin effect (up to 2× baseline) the rat-hemidiaphragm technique demands extreme technical care if it is to achieve reproducibility and thereby adequate sensitivity. Moreover, it requires the pooling of diaphragms of several animals for a given assay. Hence, it has proved satisfactory in only a few laboratories.

That insulin affects the metabolism of adipose tissue has been appreciated for some time,[8 9] and more recently it has been recognised that this effect is direct, both in vivo [10] and in vitro.[11]

In this laboratory [12] it has been found that insulin added in vitro to non-chilled, non-traumatised rat epididymal fat results in a fourfold increment in glucose uptake and an eightfold increase in the oxidation of glucose-1-^{14}C to $^{14}CO_2$. This observation has been adapted to measure insulin-like activity in biological fluids, and a technique has been developed [13] to measure quantities as small as 10 microunits per ml. (01^{-5} or 0·00001 units per ml.). Moreover, the epididymal adipose tissue from a given animal may be subdivided, giving 6 pieces (3 per side), thereby allowing comparison of insulin standards [14] and unknowns in tissue obtained *from the same animal.*

PROCEDURE

Male albino rats of the Wistar strain are fed ad libitum and killed by a blow to the head and rapid exsanguination. The epididymal adipose tissue is gently taken up at its base (just distal to the epididymal vessels), cut free (single cut), and, without manipulation or chilling, further cut into three equal pieces. Each piece, weighing 80–200 mg., is dropped, as it is cut, into appropriate 10 ml. rubber-stoppered flasks, preweighed, and containing 2 ml. of plasma or Krebs bicarbonate buffer containing gelatin 200 mg. per 100 ml. and insulin in appropriate dilutions. The glucose concentration of both buffer and plasma samples is made up to 300 mg. per 100 ml. containing 0·2 microcuries of glucose-1-^{14}C (1·9 ml. buffer or plasma plus 0·1 ml. glucose-1-^{14}C solution). The rubber stoppers are provided with two ports (glass tubing with rubber fittings) and with a small plastic cup suspended beneath one of these ports.

After reweighing, to obtain the tissue weight, the flasks are gassed (using no. 21 needles through the small rubber fittings) with 5% CO_2–95% O_2 for five minutes, the needles are withdrawn (leaving the system airtight), and the flasks are incubated for two hours at 37·6°C in a Dubnoff metabolic agitator at 72 cycles per min. After incubation, using a tuberculin syringe and no. 21 needle, 0·2 ml. of NaOH freshly diluted 1 in 10 from saturated NaOH with CO_2-free water is introduced through the appropriate port into the suspended cup, and 0·2 ml. 10 N.H_2SO_4 is introduced into the medium. After at least two hours, the contents of the suspended cup are transferred quantitatively to a weighed centrifuge tube containing $BaCl_2$, and the precipitated $BaCO_3$ is washed three times with CO_2-free water and dried and reweighed to give the total $BaCO_3$ present in the flask (usually 8–17 mg.).

An aliquot of each sample is then transferred to a weighed planchette for determination of its specific activity in a proportional flow counter, giving counts ranging from several hundred to several thousand. Results are expressed as counts per minute per total CO_2 (as $BaCO_3$) per 100 mg. adipose tissue.

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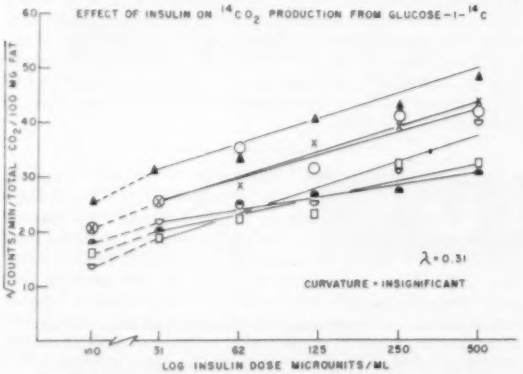
14. Supplied through the courtesy of Dr. W. R. Kirtley, Lilly Research Laboratories, Indianapolis, Indiana.

The modification using the glucose uptake as indication of insulin-like activity differs in that only 0·8 ml. of buffer or plasma is used; the glucose concentration is 200 mg. per 100 ml.; the incubation period is four hours; and sample solutions of buffer and plasma without tissue are run concurrently. Aliquots of 0·5 ml. are taken after incubation and glucose determinations are carried out in duplicate according to Nelson.[15] Results are expressed as micromoles glucose "taken up" per gramme adipose tissue.

EVALUATION

The method using CO_2 production from glucose-1-^{14}C is preferable. There are only three critical determinations —tissue weights, total $BaCO_3$ weights, and specific activity. It is feasible to carry 18 flasks (3 animals) through the procedure in one and a half days, and thus to compare in each animal 4 unknowns and 2 standards, allowing an unknown to be assayed simultaneously in 3 animals. The limit of sensitivity is 10 microunits per ml. (132% of baseline, S.E. ±4%, n=20, P less than 0·01).



Effect of insulin on $^{14}CO_2$ production from glucose-1-^{14}C.

The variation in CO_2 production in replicate tissue samples with and without insulin is 8–12%, the maximal range (lowest to highest value of sextuplicate determinations as per cent. of mean) 18–25%. The index of precision (lambda) for dose-response curves from 31 to 500 microunits per ml. is 0·31 (see figure).[16] Fasting normal plasma values range from 50 to 350 microunits per ml. Recovery of added exogenous insulin to normal plasma is satisfactorily obtained (within 20–25% of the predicted value).

CONCLUSION

It would appear that the epididymal fat pad of the male rat can be successfully used for the assay of insulin-like activity in biological fluids. This method, in our hands, has proven more sensitive, more convenient, and perhaps more accurate, than those previously described. It is, however, only a measure of insulin-*like* activity, not of insulin *per se*, and more experience is needed for a fuller appreciation of its adaptability and limitations.

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Reviews of Books

Causes of Crime

Lord PAKENHAM. London: Weidenfeld & Nicolson. 1958. Pp. 197. 21*s*.

IN 1953 Lord Pakenham undertook a comprehensive inquiry into this subject at the instigation of the Nuffield Foundation: it was interrupted after about a year by his public appointment, but he has now given us the fruits of his interim reflections. He sets out the views of a galaxy of experts interviewed during the study, and digests the findings from a number of important British writings. His conclusions are cogently argued and his opinions sound and sober, if not very controversial; and the book is easy and pleasant to read.

The main theme is, inevitably, the morass of semi-knowledge wherein we flounder. Lord Pakenham finds it easy to quote eminent authorities against each other on such basic points as, for example, the importance of intelligence or of mother's love. Variations from place to place and from time to time make it very hard to assess statistically the recent supposed increase in crime; and international comparison is even less meaningful. He points out correctly that the great majority of reasons put forward to explain this increase are, in reality, questions to which no answer yet exists: unsubstantiated emotional views hold sway and facts are at a premium. In his conclusions, however, he manages to avoid sinking into a paralysing "status agnosticus". He has a few suggestions to make about future research: most are inevitably big undertakings and only a large well-endowed and, one might add, powerful institution could achieve them. The need for the projected Institute of Criminology is inescapable and we must hope that Lord Pakenham's words will ring round the Palace of Westminster. We recommend the book to a wide public, for, though it adds little itself, it could be the starting-point for many things.

Die neuroallergischen Beziehungen in der Histopathologie der multiplen Sklerose

TIBOR LEHOCZKY, Hungarian Academy of Sciences, Budapest. Berlin: Akademie. 1957. Pp. 176.

Dr. Lehoczky has made a thorough histological study of 20 cases of multiple sclerosis. All were of the chronic progressive type, and 4 patients died during an acute exacerbation. He emphasises the predilection for the optic system, and the frequency with which sclerotic foci arise under the ependyma of posterior and inferior horns, usually separated from the ventricle by a strip of intact tissue. Acute inflammatory changes were found in most cases, mainly but not only in the periphery of foci. The constant vascular changes (hyalinisation, delamination, œdematous filling of Virchow-Robin spaces, perivascular status spongiosus, stasis, and rarely thrombosis and the formation of microgranulomata—not only near the foci of sclerosis) are judged to be an essential part of the histological changes, and not secondary phenomena; thus, the disease involves the mesenchymal as well as the ectodermal component of the nervous system.

The histological picture is compared with that of the virus forms of encephalitis and of experimental neuroallergic encephalopathy. The important investigations in Russia by Margulis and his associates, who isolated three strains of virus from acute disseminated encephalomyelitis and found that the serum of patients with disseminated sclerosis could neutralise virus, are fully reviewed, but Dr. Lehoczky failed to find in any of the reports of experimental infective encephalomyelitis a description of histological findings comparable with those in his human material. On the other hand, the changes in the encephalitis induced by injections of brain emulsion with adjuvants, which was closely studied by Rivers, Ferraro, and others in the United States and by Lumsden in this country, closely resemble those of multiple sclerosis; and the encephalomyelitis which can follow rabies vaccination (described by Japanese workers) can be considered a link between the two diseases.

Dr. Lehoczky attributes multiple sclerosis to a hyperergic antigen-antibody reaction in the nervous system—a similar view to that of McAlpine, Compston, and Lumsden. He believes that the hypothesis of Lumsden (that the antigen-antibody reaction takes place on the surface of oligodendrocytes and the inhibition of an antienzyme results in hydrolysis of the lipids of myelin sheaths) is not yet established. No attempt is made to reconcile the experiments of Margulis et al. suggesting a virus ætiology with the histopathological and experimental evidence of an allergic process.

Disinfectants

Their Values and Uses. W. E. FINCH, of the disinfectants division, Prince Regent Laboratories, London. London: Chapman & Hall. 1958. Pp. 188. 30*s*.

MOST clinicians and many bacteriologists are confused by the range of chemical disinfectants now available. Mr. Finch's book may help them to appreciate the merits and limitations of the main classes and to use them to better advantage. The coal-tar derivatives are helpfully discussed at some length, and the medical reader can learn the difference between black and white fluids—though he may be bored by the details of manufacture. Quaternary ammonium compounds and hypochlorites are well discussed in separate chapters, but mercurials and dyes, still much used in hospitals, get only a few lines each.

The chemical information is authoritative but much of the bacteriology is elementary (the glossary includes such terms as " gram-positive ", " aseptic conditions ", and " inoculate "). A chapter on methods of testing disinfectants would have been useful; there is some information about this but it is scattered through the book. The importance of using neutralisers to inactivate disinfectant carried over during testing is implied but not specifically mentioned. Five plates of general views in factories and a laboratory add to the cost of the book but not to its usefulness.

Where Love Is

JOSEPHINE BALLS, children's visitor. London: Victor Gollancz. 1958. Pp. 224. 16*s*.

ALTHOUGH relatively few children are adopted, fostered, or taken into children's homes in this country each year, they are very important for two reasons. First, the amount of care they receive is an index of the social conscience. The spirit of Bumbledom is by no means dead, and shows itself in exactly the way that Dickens satirised. " We must not be extravagant with the ratepayers' money " is the modern equivalent of " They always cost more to keep than they're worth ", and is found in the mouths of prosperous middle-class members of committees, which the 1948 Children's Act appointed to take the place of parents who, for good reasons or bad, have become unable to keep their children. All children taken into care are " deprived " children. Some of them have suffered severely, and it should be a criterion of civilised society to see that restitution is made to them. The second reason is that a study of deprived children and their disabilities throws much light on the needs of children as a whole, and helps us to understand many disturbances of health and behaviour which would otherwise be obscure. No general practitioner or pædiatrician can afford to ignore this subject.

This book is not a treatise on the law and practice of the Children's Act: it is a very readable account, by an experienced social worker (child care officer in the Children's Department of Northumberland), of the reasons which led her committee to use fostering rather than nurseries for the younger children in care. Fostering is much less expensive than nursery care, but happily the decision was not made in a spirit of parsimony, but because of a recognition that nurseries, no matter how devoted their staff, simply cannot offer young children the intellectual and emotional stimulus and response which is a necessity for the development of personality and even of physical health.

Everyone with experience of deprived children realises that prevention, not treatment, is the real answer. Most deprived children are the neglected children of inadequate parents, themselves often " deprived ". The final answer is therefore to be expressed in terms of education, premarital advice, and post-natal community support. The more immediate answer is to give what help is possible to a family threatened with disruption, and, for this, new statutory powers are being sought to enable children's officers to act. Family help service, organised by some local health authorities, is one method. The causes of neglect or non-acceptance of children, however, are many and often hard to understand. For a long time to come it will be necessary to " take children into care ". Miss Balls' book gives an excellent introduction to the subject.

Operative Surgery

Volumes 6 and 7. Editors: CHARLES ROB, M.C., M.CHIR., F.R.C.S., professor of surgery, St. Mary's Hospital Medical School, London; RODNEY SMITH, M.S., F.R.C.S., surgeon, St. George's Hospital, London. London: Butterworth. 1958. Pp. 273. 110*s*. each.

ORTHOPÆDIC surgery is completed in the sixth volume with a section on operations on the hand and another on amputations. Plastic surgery is then completely and adequately encompassed (the form of presentation, with its reliance on illustrations, is particularly apt for this subject); and gynæcology and obstetrics follow. The seventh volume presents surgery of the breast very effectively (mammoplasty is considered here, rather than in the preceding volume). In the following section on genitourinary surgery, endoscopic appearances are successfully portrayed—an important feature in the description of operations such as transurethral resection.

Modern Practice of Obstetrics (2nd ed. London: Baillière, Tindall, & Cox. 1958. Pp. 258. 45*s*.).—This edition of Mr. D. M. Stern and Mr. C. W. F. Burnett's book appears six years after the first and, like its predecessor, provides brief didactic notes rather than detailed description or argument. The chapter on antepartum hæmorrhage, for example, has been rewritten and now deals with the whole subject in 5 pages, which include an account of hypofibrinogenæmia. The use of hypotensive drugs in pregnancy is outlined, but a critical evaluation of their usefulness would have been welcome. The advances in obstetrics of the past few years are included. Some lines of treatment now discredited might, with advantage, be omitted—for instance, the use of intrauterine pastes to induce therapeutic abortion and the recommendation of frequent feeds and sweetened drinks in the management of uterine inertia. Today most authorities would regard both practices as potentially dangerous, though for different reasons, nor would they endorse the advice to leave a retained placenta, in the absence of hæmorrhage or infection, to be expelled spontaneously in the next few days. It would be wrong, however, to underestimate, by criticising details, the value of a book with so wide a range, and many will find it a useful means of revision.

Physics for the Anæsthetist (2nd ed. Oxford: Blackwell Scientific Publications. 1958. Pp. 443. 60*s*.).—Sir Robert Macintosh and his colleagues have always been active advocates of sound physical principles as the basis of good anæsthesia. Indeed probably as much progress has stemmed from a rationalisation of the art of anæsthesia, and the consequent elimination of unscientific and undesirable techniques, as from the investigation and introduction of new drugs and methods. Written to teach physics to practising anæsthetists, this book (shared with Sir Robert by Prof. W. W. Mushin and Dr. H. G. Epstein) makes the subject palatable, and the practical side is described and illustrated in a way that is entertaining and easily assimilated. Moreover, scientific accuracy has not been sacrificed. The first edition has been thoroughly revised and several additions have been made—notably, a chapter on pressure-reducing valves and four chapters on explosions, comprising nearly a third of the book. That may seem a little out of proportion, but the subject of explosions, as it concerns the anæsthetist, has never been so comprehensively or authoritatively described. This is an excellent book, well worth having and amply repaying repeated study.

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THE LANCET
LONDON 12 JULY 1958

Crime and Punishment

Lord PAKENHAM's new book, *Causes of Crime* (reviewed on p. 77), is a serious contribution to a serious subject. He would be the last to claim that it is comprehensive; the gaps, particularly in foreign research, are too wide. His advisers, however, must have helped him here, and the eclectic quality of the book does not detract from the value of its conclusions. It is saddening to realise how elusive and contradictory is our knowledge of delinquency and crime, but the reader who is disappointed at his own imperfect understanding of the roots of crime can at least take some consolation from this book—at last he knows he does not know. This reminder will do good provided it is a stimulus to renewed activity; and, although he does not discuss the matter, Lord PAKENHAM's book is powerful ammunition for those striving for an Institute of Criminology. Such an organisation would bring us into line with other countries, and, though valuable work is done at Cambridge, Oxford, the London School of Economics, the Maudsley Hospital, and elsewhere, an institute could undertake more comprehensive studies than are now possible. Do approved schools, borstals, and detention centres work? Does one type of training give better results than another? Can potential delinquents be caught young, and, if so, can we abort their antisocial activity? There are half a hundred questions of great importance to which no satisfying answer exists and to which no answer is likely to be soon forthcoming. Mr. BUTLER seems more aware of this need than other Home Secretaries have been, but the limited expansion he has achieved at the Home Office is unlikely to meet it.

The nature of the criminal act has long been the subject of bitter dispute; but, whatever may be the eternal truths underlying sin and crime, it is clear that "clinical" attitudes have slowly gained ground over the years. Now it is not always just a question of quantifying the punishment to the crime. Juvenile courts are taking the lead in recognising that some delinquents are disturbed rather than wicked children and need careful and individual consideration. Few can doubt that a young child may reflect a disturbed home life in disturbed behaviour, one form of which may be delinquency; and most of us would surely wish to pity rather than punish this victim of evil circumstance. But the delinquent child is father to the criminal man, and at what stage have we the right to change our attitude? More and more people realise that punishment per se is of less use to society and to the criminal than the creation of a person who is willing to help others instead of harming them. To excuse punishment by saying it is a deterrent has a hollow ring to those acquainted with the opposition to the earliest reforms of the death penalty. And to those who believe that the criminal act must ultimately come to be examined in its setting as a scientific problem of diagnosis and treatment (granting that the most effective treatment may sometimes be prison), Lord PAKENHAM's views will be disappointing. He believes that, for as far ahead as can be seen, conviction will be indissolubly connected with penalisation, and public opinion will not tolerate the idea of a penalty unrelated to the severity of the offence. He holds, too, that to sever this relationship would be to "embark on a slippery slope" leading ultimately to the extermination of gypsies, Jews, Catholics, or others who may be accused of damaging the best interests of the State. In company with Dr. PETER SCOTT [1] and others, we look with misgiving at the proposal to incarcerate "psychopaths" up to the age of 25, even where no offence has been committed [2]; but the recidivist criminal is another matter. Almost any proposed reform is liable to draw criticism from somebody on the ground that it will open the way to terrible consequences. But it is hard to see why, subject to rigorous safeguards, the "indeterminate sentence" should be any more a transgression against the freedom of the individual than the certification of the insane or defective is now—in fact it would probably be less so.

In reality, of course, the indeterminate sentence is with us already—in the form in which it is applied to people who are found to be both criminal and insane. It seems strange that a man who has repeatedly committed crimes of violence, only the thickness of the aorta maybe from murder, goes free at the end of his sentence, though every known prognostic index cries out that he will offend—and perhaps kill—again. On the other hand, a patient who kills in a brief confusional or depressive psychosis is locked away for life, or at any rate for years after his recovery. It is a solemn fact that men in the first group commit the spectacular murders that are in the headlines almost weekly, whereas Broadmoor patients who have been released have never killed again.[3] Public opinion (that nebulous entity called upon to justify anything) may not be as averse as Lord PAKENHAM suggests to a form of indeterminate sentence.

Œstrogen Measurement and Breast Cancer

MUCH effort is being applied to assessing and improving the effects on late breast cancer of œstrogen therapy. Encouraging progress in the quantitative estimation of urinary œstrogens is referred to in the latest two annual reports of the British Empire Cancer Campaign [4 5] and in the proceedings of a conference on endocrine aspects of breast cancer.[6] Though at present we have to make do with excretion values, what we really want to know is the amounts secreted. A step in this direction has been

1. Scott, P. D. *Howard J.* 1958, **10**, 6.
2. Report of Royal Commission on the Law relating to Mental Illness and Mental Deficiency, 1954–57; para. 367.
3. McGrath, P. G. *Howard J.* 1958, **10**, 40.
4. British Empire Cancer Campaign: annual report for 1957. Issued by the Campaign, 11, Grosvenor Crescent, London, S.W.1.
5. British Empire Cancer Campaign: annual report for 1956; p. 340.
6. Endrocrine Aspects of Breast Cancer (edited by A. R. Currie). Edinburgh, 1957.

made by BROWN,[7] who injected known quantities of œstrone, 17β-œstradiol, and œstriol into four normal menstruating women and two men and estimated the moieties excreted in the urine. The sum of these amounts was 16% of the total injected. Assuming that œstrone and œstradiol or a mixture of both is the primary œstrogenic hormone in the menstrual cycle, BROWN suggests that the amount produced in the body in each twenty-four hours may be roughly estimated by multiplying the sum of œstrone, œstradiol, and œstriol excreted in that time by a factor of $^{100}/_{16}$. The result for the sample analysed was 4·8 mg. during one menstrual cycle. This method may provide a useful guide in substitution therapy. But G. F. MARRIAN [6] has pointed out that present methods determine no more than 20–30% of œstrogen metabolites known to be present in urine. (Do some also find their way into bile and become discharged through the bowel?) In recent years four additional œstrogen metabolites have been found and characterised, and there are good grounds for believing that many more exist. Another defect, to which attention is drawn by H. BRAUNSBERG, A. E. KELLIE, J. D. N. NABARRO, and D. H. PATEY,[4] is that estimations of œstrogens at low levels (3 μg. or less) are inaccurate. Available methods have been used largely to detect and measure œstrogen excretion after attempted total ablation of endogenous sources in the palliative treatment of late breast cancer. The objectives have been to determine whether ablation has been complete; to correlate, if possible, the extent of fall in œstrogen excretion and clinical progress; and to obtain guidance on the most suitable form of palliation. Moreover, quantitative data on œstrogen secretion in the long induction period of endogenous breast cancer will be needed in order to assess the part played by hormonal factors in causation. Despite complete removal of known sources of endogenous œstrogens—the ovaries and adrenal glands—œstrogen is often found afterwards in the urine. Accessory adrenals may persist, and other sources will have to be sought. It is partly on account of the continued excretion of œstrone after these operations that hypophysectomy has been added to the surgical procedures, on the assumption that, as in the normal development of the breast both pituitary and ovarian hormones are required, so both sources may be needed for the growth of those breast carcinomas which respond to the absence of any one of them by temporary regression. Professor ILLINGWORTH's team [4] report finding no correlation between clinical progress and the extent of the fall in œstrogen excretion after bilateral oöphorectomy and adrenalectomy; and N. C. SMITH, E. BELL, and D. LINDSAY [4] detected no œstrogens after the same operations in three-fifths of the patients in whom there was good clinical response.

It is particularly difficult to account for the temporary recession of breast cancer in some postmenopausal women after administration of supplementary œstrogens. If addition of these hormones is contemplated, measurement of the existing level of excretion might afford a means of predicting which patients will benefit and of determining the dose to be given. A further problem exists in the reputed carcinogenic action of œstrogens. By methods formerly used, no correlation was found between quantities of œstrogen excreted and established breast cancer; but such an association must be sought at a much earlier stage—perhaps for twenty years or longer. This inquiry might be narrowed in two ways. First, by concentrating on reputedly "precancerous" conditions, valuable information might be gained about the likely outcome of these states.[6] Secondly, sufficient time has now elapsed since the introduction of synthetic œstrogens to look for evidence of any causal relationship with breast cancer. P. M. F. BISHOP and M. MURRAY [4] have sought to record the results of treatment of 1029 patients for periods of at least six months. Of these, only 530 could be traced and 2 only had developed cancer of target organs—in the uterus after eleven years, and in the breast after a few months' treatment with stilbœstrol. (The breast tumour is unlikely to have been initiated, though it may have been promoted, by the œstrogen.) A few other cases following œstrogen treatment have been recorded. BUCALOSSI and VERONESI [8] recorded 2 among a group of 81 patients in whom a familial incidence had been established. This observation suggests a further narrowing of the inquiry, and of œstrogen estimations, to females and males in whom a familial tendency is detected. Farsighted provision for follow-up would be needed.

It has long been known that the genesis of certain epithelial cytomas in animals is associated with naturally occurring or artificially altered hormone balances, and further that maintenance of the various growths of target cells depends on continuation of the same imbalance that brought them into existence. Little quantitative work has been done, nor is it certainly known that these growths remain dependent once they have metastasised. The exploration of this field, as was forecast by Dr. CHARLES HUGGINS in his Macewen lecture in the University of Glasgow last month, may increase our understanding of many of these problems.

Ventricular Septal Defect

VENTRICULAR septal defect in its typical form can usually be easily recognised; but the clinical picture varies considerably according to three principal factors—the size of the defect, the level of pulmonary vascular resistance, and the magnitude of the pulmonary blood-flow. TAUSSIG [9] based her classification mainly on the site of the defect. But subsequent studies suggest that it is the size of the defect rather than its position which largely determines the clinical picture; a small defect causes little hæmodynamic disturbance, whereas a large one produces large pulmonary blood-flows due to the left-to-right shunt, pulmonary arterial enlargement, and eventual heart-failure [10].

KIRKLIN et al.[11] have given a detailed account of the site of defects of the ventricular septum based on 36

7. Brown, J. B. *J. Endocrin.* 1957, **16**, 202.

8. Bucalossi, P., Veronesi, U. *Brit. J. Cancer*, 1957, **11**, 337.
9. Taussig, H. B. Congenital Malformations of the Heart. New York, 1947.
10. Selzer, A. *Arch. intern. Med.* 1949, **84**, 798.
11. Kirklin, J. W., Harshbarger, H. G., Donald, D. E., Edwards, J. E. *J. thorac. Surg.* 1957, **33**, 45.

cases in which the defects were closed surgically. They classified defects into those related to the ventricular outflow tracts and those related to the inflow tracts. The former were subdivided into those inferior and those superior to the crista supraventricularis. The latter were divided into defects beneath the septal leaflet of the tricuspid valve and those near the apex of the muscular septum. The defects unrelated to ventricular outflow tracts were located entirely in the muscular wall of the septum; but those involving the outflow tracts (referred to as high defects), although often regarded as localised to the membranous septum, often involved a large area of muscular tissue adjacent to this region. The defects confined to the muscular septum were in the minority—11 of 38 defects in 36 patients.

The hallmark of the ventricular septal defect is the passage of blood from left ventricle to right ventricle—the left-to-right shunt. When the defect is small the shunt is small and symptoms are absent, the sole abnormal physical sign being the characteristic loud pansystolic murmur at the lower end of the left border of the sternum. There is no risk of heart-failure, and the sole hazard is that of bacterial endocarditis. With larger defects, symptoms of effort intolerance and respiratory infections are common, and growth may be retarded. The heart is enlarged, and death from heart-failure may result. Clinically, in such cases it is common to find hyperdynamic enlargement of the left ventricle, and to a lesser degree of the right. The characteristic loud pansystolic murmur is heard in the third and fourth interspaces at the left sternal border; an apical mid-diastolic murmur, due to increased flow through the mitral valve, is usually audible. The arterial pulse is small and slightly water-hammer in quality. The jugular venous pressure is normal unless heart-failure is present.[12] Radiologically the heart is considerably enlarged, with dilated pulmonary arteries and evidence of increased pulmonary blood-flow. The cardiogram shows greater hypertrophy of the left ventricle than of the right. Cardiac catheterisation reveals a large left-to-right shunt at ventricular level, normal arterial oxygen saturation, and normal, or near normal, pulmonary arterial pressure and resistance: the large pulmonary blood-flow is accommodated in the distensible pulmonary vascular bed without a rise in pressure. In some cases the Eisenmenger syndrome is present. This has been defined as pulmonary hypertension with high pulmonary vascular resistance and reversed shunt.[13] In such cases the left-to-right shunt is small or absent, a right-to-left shunt is present, and the clinical picture is one of extreme pulmonary hypertension with slight central cyanosis and clubbing. The mitral diastolic murmur disappears and the sound of the pulmonary valve closure is much increased. The cardiogram shows pure or dominant right ventricular hypertrophy, and the peripheral vascular markings in the lung may be reduced.[13 14] According to WOOD [13] the high vascular resistance is present from birth, and thus the clinical picture is entirely different from that of the large defect with left-to-right shunt and normal pulmonary vascular resistance. The right-to-left shunt in ventricular septal defect was originally attributed to overriding of the aorta, which received blood from the right ventricle. It is now considered that the right-to-left shunt results solely from increased pulmonary vascular resistance, which is at or near systemic level, when the aorta becomes "physiologically" overriding.[10 13] SELZER and LAQUEUR [15] suggested that there is no anatomical difference in the heart between uncomplicated ventricular septal defect and the Eisenmenger complex (better termed syndrome). The difference lies in the presence, in the latter condition, of reduced calibre of the pulmonary arterioles and consequent high vascular resistance. In any form of ventricular septal defect the aortic root may occupy its normal position, or may be overriding, or even partly or completely transposed.[15] Both WOOD [13] and SELZER and LAQUEUR [15] agree that the septal defect in the Eisenmenger syndrome measures 1 cm. or more in diameter, which in the infant is of considerable size relative to the size of the heart.

A valuable study of the natural history of ventricular septal defect has been made by BROTMACHER and CAMPBELL,[16] who have analysed 75 cases. They classified these into five groups: small defects with small left-to-right shunt (3–3·5 litres per min.); larger defects with a left-to-right shunt of 4–15 litres per min. but with normal pulmonary-artery pressure; larger defects with considerable left-to-right shunts, and hyperkinetic pulmonary hypertension due to extreme flow rather than increased resistance; large defects with some increase in resistance but no reversal of shunt; and finally large defects with right-to-left shunt, in which the aorta is "functionally overriding". They regard the *maladie de Roger* and the Eisenmenger complex as the two extremes of a continuous series of cases of ventricular septal defect, and recommend that both eponymous terms be abandoned. Nearly three-quarters of their patients were under 20 years of age, and the sex distribution was equal, but the prognosis was considered to be worse in boys and men than in girls and women. BROTMACHER and CAMPBELL thought that the pulmonary vascular resistance tended to rise with age, in that the average age in the high-resistance cases was higher than that in the low-resistance cases. They consider that the pulmonary-artery pressure is usually high from birth; the hypertension at first is mainly hyperkinetic, but the resistance increases with age, as BLOUNT et al.[17] concluded. This is not in close harmony with WOOD's [13] view that the high vascular resistance is determined from birth. BROTMACHER and CAMPBELL [16] cite the case of a patient whose pulmonary vascular resistance was 8 units at the age of 5 years, and had risen to 23 units seven years later; but they do not believe that the pulmonary-artery pressure is likely to rise as a late complication in patients in whom it was initially normal. It may be, therefore, that the pulmonary vascular resistance is likely to rise

12. Wood, P., Magidson, O., Wilson, A. O. *Brit. Heart J.* 1954, **16**, 387.
13. Wood, P. Diseases of the Heart and Circulation. London, 1956.
14. Doyle, A. E., Goodwin, J. F., Harrison, C. V., Steiner, R. E. *Brit. Heart J.* 1957, **19**, 353.
15. Selzer, A., Laqueur, G. L. *Arch. intern. Med.* 1951, **87**, 218.
16. Brotmacher, L., Campbell, M. *Brit. Heart J.* 1958, **20**, 97.
17. Blount, S. G., Jr., Mueller, H., McCord, M. C. *Amer. J. Med.* 1955, **18**, 871.

with age only if it is initially increased. These workers make valuable comments on lesions associated with ventricular septal defect. Pulmonary regurgitation was diagnosed in 19 of the 75 patients, being nearly three times as common as in atrial septal defect. The pulmonary pressure was increased in all save 1. Aortic regurgitation was present in 3 patients, 2 of whom died; and BROTMACHER and CAMPBELL regard this as a much more serious complication than pulmonary regurgitation. The aortic arch was right-sided in 2 patients, and at least 3 had a left superior vena cava. Changes of rhythm were uncommon; atrial fibrillation occurred in 1 man, and congenital heart-block in 1 woman, who was cyanotic. The report refers briefly to 8 patients who were not included in the series because of a small pressure-gradient across the pulmonary valve, which was not attributed to pulmonary stenosis. This " functional " gradient is now well recognised, as in atrial septal defect, in which the exact cause is not known.[18]

The course and prognosis were analysed with reference to a further 100 patients who had not been investigated by cardiac catheterisation. 11 patients died, 9 of them before the age of 25; 6 of these 9 died in childhood (1 at the age of 3 years), having enormous hearts, considerable left-to-right shunts, and heart-failure. The tendency for patients with large left-to-right shunts to die in infancy is now established [19]; and BONHAM-CARTER and WATERSTON [20] reported that two-thirds of a series of 200 patients with congenital heart-disease who died in infancy from acute cardiac illness did so under the age of 6 months. Some of these patients presumably had ventricular septal defects, and it may well be argued that the principle mortality from this condition lies in the first year of life. BROTMACHER and CAMPBELL [18] point out that if the patient survives infancy the prognosis is moderately good for fifteen years, but unless the shunt is small the outlook becomes progressively worse after this age, and few patients survive to 40 years. A high infant mortality in ventricular septal defect would accord with WOOD's [13] contention that patients in whom the high fœtal pulmonary-vascular resistance falls to normal soon after birth are in serious danger of death from heart-failure. He goes further and suggests that in many cases the high pulmonary resistance of Eisenmenger's syndrome is life-saving, as it prevents the lungs being flooded with blood under systemic pressure and protects the left ventricle from the burden of the large left-to-right shunt. The prognosis of the Eisenmenger complex is fair. Of 35 fatal cases reported by SELZER and LAQUEUR,[15] 8 patients died in infancy, 4 between the ages of 3 and 10 years, and the remainder subsequently—1 patient living to the age of 60. 19 patients survived to between the second and fourth decades; so there is a reasonable chance of a patient living to the age of 30, which agrees with BROTMACHER and CAMPBELL's findings regarding ventricular septal defects of all types if the hazard of infancy is survived. The high risk of infective endocarditis in ventricular septal defect is worth remembering: it accounted for 28% of the deaths over the age of 1 year in SELZER's [10] series, although it was not a prominent feature in the series of WOOD et al.[12]

The surgical treatment of ventricular septal defect is now well established. KIRKLIN et al.[11] have reported excellent results in 36 cases, and the number is probably now much higher. Closure requires the use of an extracorporeal circulation while the heart is opened and the defect closed, and the operation is therefore only possible in special centres. The indications for operation are a left-to-right shunt which is producing significant cardiac enlargement or effort intolerance, and early heart-failure. Preferably the pulmonary pressure and resistance should be normal; but some hyperkinetic hypertension is no bar to operation, as the pressure will fall when the shunt is closed. Since many patients probably die in infancy operation may prove to be most valuable when undertaken while the patient is in the first year of life. The risks of operation are much greater when the pulmonary pressure and resistance are high and the shunt is reversed than in uncomplicated ventricular septal defect; and ZIMMERMAN et al.[21] suggest that the pulmonary-artery pressure should ideally be below 75% of the systemic arterial pressure if closure is to be effected safely.

18. McDonald, L. *Brit. Heart J.* 1958, **20**, 268.
19. Marquis, R. M. *ibid.* 1950, **12**, 265.
20. Bonham-Carter, R. E., Waterston, D. *ibid.* 1958, **19**, 589.
21. Zimmerman, H. A., Kay, E. B., MacKrell, J., Sambhi, H. P. *Amer. Heart J.* 1957, **54**, 727.

Annotations

ASSESSMENT OF DISSEMINATED SCLEROSIS

DISSEMINATED sclerosis is diagnosed largely on the pattern of the disease in time and space. But the characteristic picture of episodes of neurological dysfunction with partial or complete remission between—the episodes involving different areas of the nervous system or recurrent and increasing dysfunction of the same area—is by no means consistent. A spinal form was early recognised as having a slowly progressive course without remissions and often without clear evidence of spatial dissemination. In cerebral forms, too, an initial attack may be followed by steady deterioration. In other cases a single attack is followed by complete and long-continued remission (even, occasionally, with no further recurrence) or by a series of attacks with complete remission between. Other patients show increasing permanent disability after each attack. In still other cases, perhaps the commonest, there is complete remission from each attack for a time and then a steadily progressive phase. Examples of all these varieties have been confirmed at necropsy. Thus if histological evidence of plaques of demyelinisation with profuse astrocyte infiltration and characteristic relation to blood-vessels and grey matter is accepted as pathognomonic of disseminated sclerosis, such patients must be regarded as having that disease. After the first five years all forms of the disease show a tendency to become steadily progressive, and there is some evidence that, apart from the variations already mentioned, in general the disease may take either a relatively benign or an inexorably progressive form.

These features make diagnosis and prognosis difficult and the assessment of treatment even more so. If any remedy were truly curative, this could hardly escape detection; but if the effect were simply to slow down or

modify the disease process, this would be less easily appreciated. Conversely with treatment instituted around the fifth year apparent benefit might really be due to natural decline in relapses and remissions as the disease enters a chronic progressive phase.

Experience with the various remedies has illustrated these difficulties. Of the older remedies arsenic is still advocated despite the occasional tragedy of arsenical epitheliomas. Administered for periods of years, it is claimed to bring about cessation of relapses; but in many cases, however treated, relapses cease after five years. Fever and shock therapies are less popular now; anticoagulants, anti-histamines, and low-fat diets, although not widely accepted, have their adherents.

In this situation the carefully matched control series may be particularly helpful. The recent report of Alexander et al.[1] from Boston is therefore welcome. They studied a group of 554 patients with disseminated sclerosis over an eight-year period and confirmed that the peak incidence is in the third decade, the disease being largely confined to the 20–40 age-group; that the frequency is greater in women than in men; that the disease tends to become less active after the first five years; and that there are probably two groups—a mild and a severe. The particular merit of this report is its emphasis on the need for a quantitative estimate of disability and for assessing treatment against a control series matched not only for age, sex, length of illness, and condition at the start of treatment but also for quantitative illness record for a year before treatment. Four treatments were thus investigated: vitamins plus muscle adenylic acid, blood-transfusions, corticotrophin, and cortisone. Of these, transfusions appeared to aid in resolution of attacks, while corticotrophin aided resolution and both prevented and reduced frequency and severity of subsequent attacks and reduced progressive disability between attacks. The others had no significant effect. The claim, which contrasts with the admittedly less extensive experience of other workers, that corticotrophin beneficially affects all aspects of the disease process will certainly lead to further clinical trials. Let us hope these also will be so controlled that the results are meaningful.

COMPLEMENT AND STIMULANT

THE Nuffield Provincial Hospitals Trust was founded in 1939 with the main purpose of coordinating hospitals and ancillary medical services on a regional basis. This objective was largely fulfilled with the start of the National Health Service; but in the second decade of its short life the Trust has done work no less valuable than in the first decade.

Coordination is still the principal aim; and this is reflected in the financing by the Trust of the development of group-practice and clinic centres at Harlow. As a large voluntary agency, the Trust complements and stimulates official action by discovering facts on which official policy may be based, and by encouraging the practice of promising but unproved ideas. In these ways such a body as the Trust can go far towards preventing the conservatism and rigidity often seen in activities paid for from Exchequer funds. A report on the work in the past three years [2] remarks sensibly "that a trust must be careful not to duplicate work best done by public authorities. . . . Above all, it has a duty to be far thinking and try to interpret its objectives in relation to the requirements of the times. Its policy, if not opportunist, must be as flexible as its trust deed permits." How well this Trust is succeeding is evident from the list of projects, established and new, that have gained its support.

The trustees are continuing to support an exhaustive study of the administration of the National Health Service, which is being published by the Acton Society Trust. New projects under organisation include further studies of hospital case-loads, to provide a basis for planning; follow-up studies of the working capacity and needs of patients discharged from hospital; and an investigation into the use of health and social services. Of special interest and importance is a grant to help in planning to bring into use the new Princess Margaret Hospital at Swindon. A working party is studying all aspects of the operation and will record its findings for the benefit of any hospital authority that has a similar, sadly unfamiliar, duty. Many further projects sponsored or supported by the Trust are listed under organisation and the further headings of mental health services, care of the aged, rehabilitation services, general practice, industrial health, training and education, and design and operation.

BRONCHOGRAPHY IN PULMONARY TUBERCULOSIS

VARIOUS workers, notably Dormer et al.,[1] have studied the use of bronchography in pulmonary tuberculosis; but until recently the method was little applied in this condition, partly owing to the danger of extending the disease, and partly because residual unabsorbed oil obscured further radiographs. Chemotherapy and the introduction of a new contrast medium, propyliodone ('Dionosil') have changed all that. Except in patients with a persistently positive sputum due to drug-resistant organisms, the risk of the disease being spread after adequate chemotherapy has practically vanished, and the contrast medium disappears promptly from the lung fields; furthermore because, in the new medium, iodine is in organic combination, the rare tragedy due to iodine-sensitivity is no longer liable to occur.

The routine use of bronchography in cases of pulmonary tuberculosis where surgery is contemplated has also been favoured by the increasing recognition of the limitations of the ordinary radiograph. While these limitations are in some degree overcome by tomography—lateral sections are particularly helpful—the bronchi themselves can be properly delineated only by a contrast medium; and the importance of the bronchus as a factor in the physiopathology of pulmonary tuberculosis is now more fully appreciated. Furthermore the tendency is to resort less often to bronchoscopy, partly because lesions in the major bronchi are known to heal readily with chemotherapy, partly because the lesser bronchi cannot be seen, but principally because bronchography is such an efficient method of "lung-mapping" that in most cases bronchoscopy is unnecessary. Bronchography is less upsetting than bronchoscopy with local anæsthesia; and general anæsthesia is necessary only in young children. The contrast medium itself is relatively non-irritating, although a mild febrile reaction may ensue.

Most thoracic surgeons contemplating resection for pulmonary tuberculosis now routinely request preoperative bronchography; it is of value sometimes in the investigation of "round shadows" which may be

1. Alexander, L., Berkeley, A. W., Alexander, A. M. *J. Amer. med. Ass.* 1958, **166**, 1943.
2. The Nuffield Provincial Hospitals Trust: a record of the progress of schemes and descriptions of new projects. 1955–58. Issued by the Trust, Nuffield Lodge, Regents Park, London, N.W.1.

1. Dormer, B. A., Friedlander, J., Wiles, F. J. *Amer. Rev. Tuberc.* 1944, **50**, 283, 287; *ibid.* 1945, **51**, 62, 455, 519.

either tuberculous or malignant, as with the latter a distant "block" may be apparent; and anatomical variations from the normal bronchial pattern can be demonstrated preoperatively. Merrill and Sampson,[2] analysing a series of bronchograms of their tuberculous patients in 1956 at the Highland-Alamida Hospital, Oakland, California, point out that pathological examination of resection specimens has contributed to diagnostic accuracy and that changes in the segmental bronchi are comparable with those in the major bronchi. They are, however, critical of the view which accepts the mere presence of ectatic bronchi as an indication for resection; resected specimens of these bronchi are not uncommonly smooth-walled and non-caseous, which would seem to indicate that little harm would have resulted if the decision had been against operation. As the effectiveness of properly managed long-term chemotherapy becomes ever more evident, the indications for operation are becoming fewer and less clear-cut. The presence of distinct stenosis may indicate the need for surgical intervention, as in the "middle-lobe" syndrome or where an empyema space communicates with the bronchus. But there is still a real need for accurate assessment of the results of long-term chemotherapy; and we cannot yet prognosticate clearly from the bronchographic picture regarding patients with ectatic bronchi in whom control appears to have been achieved by chemotherapy. There is of course some risk of secondary infection, though it does not seem to be great; of hæmorrhage, though this is apparently unusual; and of recrudescence of disease, though this depends also on other factors such as the presence of cavities, round foci, and apical deposits, besides general factors, including inherited resistance and constancy and duration of chemotherapy.

CANCER CONGRESS

SOME 2500 members and associates from more than sixty countries enrolled for the seventh International Cancer Congress, held in London this week under the presidency of Sir Stanford Cade, who read a message from the Queen, the congress patron. The congress was opened on Monday by the Duke of Gloucester; and the meetings, of which we hope to give some account, were continuing until Friday.

TREATMENT OF TROPICAL EOSINOPHILIA

THE syndrome of tropical eosinophilia (pulmonary eosinophilia, eosinophilic lung) is familiar to practitioners in Asia. The patient is an Indian with paroxysms of coughing specially at night, added sounds on chest auscultation, significant eosinophilia, and increased shadows in the chest radiograph. The cause is unknown, but arsenical treatment is usually successful. Other features, which are variable, include asthma, chest pain, scanty hæmoptysis, insomnia, fatigue, weight loss, and—specially in children—enlarged lymph-glands and liver. Fever is usually slight or absent, but the erythrocyte-sedimentation rate is increased. The onset is typically insidious and the illness continues with remissions for weeks, months, or years—up to twenty years has been recorded.[3] There are a host of causes and degrees of eosinophilia in the Tropics, but many clinicians regard tropical eosinophilia as a clear-cut entity. On the other hand, Aitken and Roy,[4] in their study of 200 cases on a Bengal tea estate, found that the symptoms were protean; and the majority had no symptoms at all. Gelfand[5] encountered similar cases in Rhodesia. Aitken and Roy suggested that hospitals saw selected examples of a syndrome which was confined neither to the Tropics nor to the lungs, and suggested the term "eosinophilic syndrome group".

In treatment organic arsenicals, which are usually effective, may have to be given for six to eight weeks. The main drawback is toxicity—especially arsenic encephalopathy, which is often fatal. Such an outcome is particularly unfortunate in an illness which is not fatal in itself. Danaraj[6] considers that toxic reactions are commoner than published reports would indicate. He therefore studied the effects of other empirical measures, including antibiotics, sulphonamides, bismuth, cortisone, piperazine, and diethylcarbamazine. Only diethylcarbamazine produced results comparable to those of arsenic. Diethylcarbamazine was advocated by Friess et al.,[7] who found *Wuchereria malayi* in lymph-nodes of six soldiers returning from Indo-China with tropical eosinophilia; and earlier reports of the use of this drug were favourable.[8–11] In Singapore Danaraj[6] has studied the effects of diethylcarbamazine in 110 patients of whom 90% were male, over 80% adult (in other series, children and females have predominated), and over 70% Indian—although Indians form only 7·8% of the population of Singapore. Selection criteria were an eosinophil-count of over 3000 per c.mm., increased shadows in the radiographs, an erythrocyte-sedimentation rate of more than 10 mm. in the first hour, and no evidence of past or present filarial infection. Dosage was 4 mg. per kg. thrice daily for four days in 46 cases, and 6 mg. and 10 mg. per kg. body-weight thrice daily for five days in 57 and 7 cases respectively. The patients were observed, mostly as out-patients, for an average period of six months. Symptoms improved within two to four days of treatment being started, but the response was better with the two larger dosages than with 4 mg. per kg. Giddiness and frequent vomiting occurred in 6 of the 7 patients given the 10 mg. per kg. dose; and Danaraj therefore recommends 6 mg. per kg. body-weight thrice daily for five days as the standard dosage. Eosinophils fell to below 3000 per c.mm. in five to thirty days according to the initial level. The chest radiograph cleared more slowly, and the erythrocyte-sedimentation rate was still increased in 25 patients at the end of the period of observation. Only 1 patient—1 of 17 Chinese—showed no response. 3 patients had relapses.

These results are very encouraging, particularly as diethylcarbamazine is relatively non-toxic. The results would have been even more convincing if a double-blind controlled trial had been carried out. As the syndrome is relatively common in India and Malaya, such a trial should be readily feasible. Last year Gault and Webb[12] reported finding nematode larvæ in the liver of a patient with tropical eosinophilia; but full understanding of the cause—if in fact there is a single cause—continues to elude us.[13] Why is the syndrome in Malaya virtually confined to Indians? Does a genetic or dietary factor make the Indian more susceptible to a parasitic infection? Why is the cough so persistent at night? Lung biopsy at night might reveal the answer.

2. Merrill, D. L., Samson, P. C. *ibid.* 1958, **77**, 561.
3. Ball, J. D. *Trans. R. Soc. trop. Med. Hyg.* 1950, **44**, 237.
4. Aitken, W. J., Roy, K. P. *ibid.* 1953, **47**, 419.
5. Gelfand, M. *ibid.* 1956, **50**, 283.
6. Danaraj, T. J. *Quart. J. Med.* 1958, **27**, 243.
7. Friess, J., Pierrou, M., Segalen, J. *Bull. Soc. Path. exot.* 1953, **46**, 1037.
8. Wildervanck, A., Winckel, W. E. F., Collier, W. A. *Docum. Med. geogr. trop.* 1953, **5**, 67.
9. Ganatra, R. D., Lewis, R. A. *Indian J. med. Sci.* 1955, **9**, 672.
10. Chaudhuri, B. N. *J. Indian med. Ass.* 1956, **27**, 195.
11. Danaraj, T. J. *Proc. Alumni Ass. Malaya*, 1956, **9**, 172.
12. Gault, E. W., Webb, J. K. G. *Lancet*, 1957, ii, 471.
13. *ibid.* p. 478.

Special Articles

TEN YEARS' GROWTH OF THE WORLD HEALTH ORGANISATION

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IT is interesting to recall the mood of 1945 and 1946 which led to the launching of the United Nations Organisation and some of its specialised agencies.[1] The world, reacting to the misery and disturbance of the war, was ready for, indeed expecting, concerted action to give all peoples fuller and better lives. The emergence of the atom bomb and the talk then of fearsome biological warfare also impelled a search for closer international cooperation in resolving quarrels and removing their causes. The widespread prevalence of want and disease were believed to be prominent among such causes. Hence the urgency to extend international association in functional fields as well as in those of traditional diplomacy.

As regards health, this mood simplified the acceptance of principles long advocated:

1. A single international body to coordinate health affairs.
2. Membership to be universal.
3. Functions to be comprehensive—i.e., not limited to quarantine and similar traditional functions.

Now that ten years have passed since the first World Health Assembly met in Geneva in July, 1948, examination of the application of these principles should be instructive.

Membership

During that first Assembly of the World Health Organisation, the ratifications of the constitution brought the membership of Governments to 55. Further ratifications and the accession of new countries have now increased the membership of W.H.O. to 85 members and three associate members. The only intergovernmental agencies with more comprehensive membership are the Universal Postal Union (96) and the International Telecommunications Union (91).

In 1949 and 1950 the Governments of Soviet Russia, the Ukraine Republic, Byelorussia, Bulgaria, Rumania, Albania, Czechoslovakia, Hungary, and Poland, informed the Organisation that they no longer considered themselves members of the Organisation; but, as the constitution makes no provision for withdrawal, they were regarded as " inactive ". In the year ending last January the Soviet Union, Poland, Czechoslovakia, Bulgaria, Albania, and Rumania, resumed active membership.

Structure

Ten years ago there were a headquarters in the Palais des Nations at Geneva; a liaison office in the United Nations headquarters in New York; and an epidemiological quarantine office, taken over from the League of Nations, in Singapore.

Despite some initial doubts about the wisdom of its early application, the principle of regionalisation was put into effect immediately. The world was divided into six regions, and by 1951 regional organisations were operating in all. These now have headquarters as follows:

African Region	Brazzaville
Region of the Americas	Washington, D.C.
South-East Asia Region	New Delhi
Eastern Mediterranean Region	Alexandria
European Region	Copenhagen
Western Pacific Region	Manila

1. Gear, H. S. *Brit. med. J.* 1956, ii, 471.

The Americas had long had their own regional health body in the Pan-American Sanitary Organisation, with its bureau headquarters in Washington. By an agreement of 1949 the P.A.S.B. assumed its role of the regional office of W.H.O. Each of the regional offices has grown with the years and now keeps in close contact with the health authorities of its region.

The trend of decentralisation has not stopped with the establishment of the six comprehensive regional offices, each operating with its appropriate regional committee of local Governmental representatives. A varied system of subdivisions has appeared.

In the African Region there are four areas under the supervision of public-health officers.

Even before the advent of W.H.O. the Region of the Americas had zone offices in Guatemala City and Lima. It now has six zones, each with its own headquarters.

In the South-East Asia Region there are five area representatives stationed in Burma, Ceylon, India, Indonesia, and Thailand.

The European Regional Office has not yet any geographical subdivisions. In 1956 the Eastern Mediterranean Office appointed four public-health advisers to coordinate the programmes in Libya, Saudi Arabia, and Yemen; Ethiopia, Sudan, and Somalia; Iran, Iraq, and Pakistan; and Jordan, Lebanon, and Syria. In view of the present suitability of this arrangement, a scheme for area representatives has not yet been put into force. Area representatives have, however, recently been appointed for three groups of countries, and a fourth is to be added soon in the Western Pacific Region.

Thus ten years' growth has led to a large, even complex, system of regionalisation, with subdivisions undertaking the general programme and administrative functions of the Organisation in the individual countries of the world.

A Decade of Programmes

The programmes fall into three broad groups, though in practice these have not always remained distinct.

(1) *General Technical Services*

The general technical services are given to the world as a whole. These are the traditional services which countries have found it essential to seek from an international body. They arose to meet the need for common understanding and action on the terminology and classification of the causes of mortality and morbidity; on the description of drugs and related substances; on the definition of the agents and causes of diseases, microorganisms, &c.; and on the quarantine procedures acceptable for international traffic.

This traditional work has been maintained and extended by W.H.O. The International Lists of Diseases, Injuries and Causes of Death have twice been revised under its ægis. These are now being applied by many more countries in a continuing effort to produce fuller and more accurate records of both mortality and morbidity, without which health and medical programmes are liable to be aimless and wasteful. This basic statistical work has contributed much in all regions to preliminary programmes of world epidemiology. Epidemiology, in the full modern sense of the word—a study of factors influencing the health of a community—has emerged as an essential responsibility of W.H.O. Statistical data are but part of the epidemiological information needed on world and regional conditions. In such subjects as malaria, tuberculosis, poliomyelitis and the other virus diseases, " cancer ", circulatory conditions, accidents, and mental disease much additional epidemiological work has been done. In most cases the prosaic but essential preliminaries

have first been taken: nomenclatures and classifications have been prepared; arrangements have been made for reference material, bacterial types, &c., to be distributed; and basic clinical, pathological, and therapeutic definitions have been reached. Thus the way has been prepared in many countries for the application of modern measures. The common understanding now being found in these basic statistical and epidemiological criteria has also meant an expansion in both the number of subjects and the geographical areas in which investigation is proceeding as a cooperative arrangement. The work on malaria, bilharziasis, and enteric infections are examples of how world cooperation in research has been much helped by the agreements on nomenclature, reference material, and technical descriptions sponsored by W.H.O.

Another example of general action is in the health procedures for international traffic. The last few years have seen significant reductions both in the prevalence of the so-called quarantinable diseases and in the oppressive and obstructive measures previously applied to shipping, aircraft, passengers, and goods in order to prevent their spread. We now know more about the epidemiology of cholera, smallpox, plague, typhus, and yellow fever, and the argument that barriers are effective against them—quarantine inspection, holding of ships and aircraft, quarantining of passengers—is less often used. We now believe that quarantine systems have played a relatively small part in reducing their world importance: local measures taken by individual countries—e.g., better water-supplies, disposal of waste products, cleaner towns and ports, and ships properly constructed and kept free from rats, &c.—have been usually more effective. This refreshing change in attitude has enabled the old Sanitary Conventions, so hampering to world movement, to be superseded by the much less restrictive International Sanitary Regulations of 1952.[2] To resist cholera, plague, and the rest, countries increasingly depend on their own internal sanitary condition rather than on the doubtful defence of quarantine.

Another action taken through W.H.O. which has had both medical and economic advantages has concerned the international and local use of drugs, antibiotics, and the like. In most countries the practitioner and the pharmacist use drugs—diagnostics, prophylactics, and therapeutics—which have been manufactured in other countries, and there is obvious need for generally intelligible and acceptable dosage standards governing potency, purity, and safety. Early efforts made by the League of Nations have been carried forward, often with the assistance of W.H.O., and recommendations are made, for example, in the *International Pharmacopœia*.[3] A list of international non-proprietary names is helping to decrease the confusion caused by the labels—often different in different countries—given to new medicinal substances. It has helped manufacturers as well as doctors.

The international work on biological standardisation, also initiated by the League of Nations Health Organisation, has been much accelerated by W.H.O. By 1945, when W.H.O. took on this work, thirty-four international biological standards—in such substances as digitalis, vitamins, antitoxins, and antisera—had been established. In the past ten years another fifty have been prepared. This again assists the manufacturers and distributors as well as the users of these substances. The international standards are held, on behalf of W.H.O., in the Statens Seruminstitut, Copenhagen, and the National Institute for Medical Research, London.

2. Gear, H. S., Deutschmann, Z. *Chron. World Hth Org.* 1956, **10**, 273.
3. Pharmacopœia Internationalis. Geneva, 1951.

(2) *Education, Training, and Technical Information*

Several allied programmes may be described together in this group. Governments have sought much guidance and help in the fields of medical education and technical information. Indeed, in a sense, all services provided by W.H.O. for its member countries have had, as a main objective, education and the diffusion of information.

Countries eager to develop their own medical schools, and to provide themselves with the advantage of modern medicine and public health, have made use both of the W.H.O. fellowship system (for training their own people) and of the arrangements for obtaining advice from experts who may visit them individually or in groups. The fellowship programme—much indebted to earlier international schemes, including those of the Rockefeller Foundation—has been prominent among W.H.O. activities throughout the decade.

In 1947–56 6396 fellowships were granted to people from 149 countries and territories. These fellows went to 113 other countries to receive training—almost always postgraduate. The subjects studied were health services by 59%, control of communicable diseases by 28%, and medical education, clinical science, and other subjects by 13% of the fellows.

The fact that W.H.O. fellowships are now being used each year by nearly 1000 medical and allied people makes this one of the most significant postgraduate training schemes ever developed. Countries are thus getting knowledge and skill to guide their own advances. A large number of training institutes (universities, medical schools, research laboratories) receiving W.H.O. fellows have become partners in the diffusion of experience and information.

This movement of fellows, and the reverse flow of teachers and consultants, in so many countries and territories, must have effects beyond the specific training for which they were designed. Their influence in drawing at least medical and technical communities of the world together, in creating common traditions and associations, and in giving common standards, practices, and languages, will probably continue to radiate good will and community of purpose for many years after the actual exchanges.

It is too trite to claim again the value of publications in diffusing scientific and technical knowledge. A whole series has been developed by W.H.O. for its international purposes.

Most originated in the League of Nations Health Organisation or in the Office International d'Hygiene Publique. These have been issued in terms of the publication policy laid down by the Health Assembly and the Executive Board, which requires material to be selected for publication which has a direct relation to international medicine or health. Thus the quarterly *W.H.O. Bulletin*, its principal scientific journal, has included articles on laboratory studies on communicable diseases, control of disease, geographical distribution of disease, surveys of regional or world health and medical subjects, and reports of W.H.O. field projects.

Epidemiological and statistical data have been presented in monthly and annual reports to furnish essential material for research-workers and medical administrators everywhere. Over thirty years of reports now make a valuable repository of world medical and health facts, incomplete and uneven in quality though the material still is. The issue of summaries of national health legislation has been a routine practice for several decades, appealing mainly to certain official groups. The introduction in 1952 of comparative surveys of legislation on such subjects as smallpox vaccination, nursing, leprosy, malaria, and midwives has enlarged the usefulness of the

publication in question, *The International Digest of National Legislation*. It has become a ready reference for medical administrators, practitioners, and others concerned in keeping the legislation of their own countries adapted to modern technical and administrative requirements.

W.H.O. technical publications—one, the *Chronicle*, in the five official languages (Chinese, English, French, Russian, and Spanish) and others in English, French, and Spanish—help scientific and technical institutions and people throughout many countries to keep in touch with subjects of importance to international health. They offer accessible guidance and reference to many medical and health groups concerned in international programmes and services. So far, they have been carefully directed to be complementary to, and not in competition with, the well-known medical and health journals of international appeal published in a number of countries.

(3) *Country Project Work*

This third group of activities has been the most prominent in the first ten years of W.H.O. It became so to meet insistent demands from its member Governments for advice and help in creating new, or expanding existing, country health and medical services. These requests have varied from a simple need for a visiting consultant (to advise a country for a few days on a single subject) to a complex agreement between W.H.O. and associated international agencies to help a country over a period of years in establishing a whole health department or such a special service as tuberculosis control or a new medical teaching faculty. This has been the type of service most enlarged by all international agencies in recent years. It has been the main activity not only of the United Nations family of specialised agencies but also of vast programmes conducted under the aegis of the Colombo Plan, and the various bilateral arrangements sponsored by the United States of America. In the case of W.H.O., this form of direct assistance to individual countries making requests has grown substantially. In 1949 the direct expenditure on such advisory services was 2,199,456 dollars. In 1957 it was 12,024,699 dollars—by far the largest item of expenditure.

This form of aid to Governments is popular. It is so in all W.H.O. Regions and in all medical and health fields—clinical, preventive, and investigational. Through it and the allied bilateral programmes (Colombo Plan, T.C.A., &c.) the last ten years have witnessed the rudiments of health and medical services growing in practically all countries. Modern scientific medicine, through general practitioners and hospital, through training institutions, and in many cases through special services to deal with malaria, yaws, and the like, has been extended into the most primitive communities. It was to meet a fundamental principle that the advisory services given by W.H.O. have been directed towards strengthening the local national and local services and not towards creation of new institutions and departments detached from the local political and administrative systems. The aim has been to induce self-help, adjusting aid from outside to internal conditions, customs, and needs.[1]

Expenditure

Expenditure is an obvious index to programme and administrative change year by year. But the annual expenditure is not always a complete reflection of trends, because it is affected by such factors as changes in the value of currency, special non-recurring commitments, and emergencies.

The annual financial reports of W.H.O. reveal an uninterrupted increase in expenditure for the decade. The first full programme year, 1949, showed an expenditure of 6,005,629 dollars, and the most recent, 1957, an expenditure of 17,681,877 dollars. In other words, in the ten-year period the costs of the programme and administration have roughly trebled.

The expenditure has been met by income from several sources, but most of these have been relatively minor. Most of the regular annual income has come from the member States directly. These contributions from Governments, according to an agreed scale of assessments, rose from 3,693,603 dollars in 1949 to 11,517,988 dollars in 1957.

The annual expenditure in 1957 has been classified as follows:

	(*Dollars*)
Organisational meetings	373,361
Operating programme	15,925,260
Administrative Services	1,383,256
Total	17,681,877

In the first year, 1948, about 66% of the assessments were collected in the year, but since 1951 the collections have been 90% in each year; and for 1957 the proportion was over 97%. This is practical evidence of vigorous participation by Governments in the work of the Organisation, without which there would be uncertainty, confusion, and haphazard effort.

The programmes of the Organisation have also benefited much from the contributions made by two funds: the United Nations Expanded Programme of Technical Assistance for Economic Development of Underdeveloped Countries, and the United Nations International Children's Fund (UNICEF). In each country with a W.H.O. project there has been counterpart expenditure to pay for the local personnel, transport, supplies, &c., necessary to complete or continue the new or improved service.

Staff

The World Health Organisation took over a staff of 206 from the interim commission which had continued essential work and plans in the period between the International Health Conference 1946 and the first World Health Assembly in 1948. Many of these had previously worked in the earlier health bodies of the League of Nations, &c. Ten years later, in 1958, the staff numbers 1481, distributed as follows:

Headquarters and attached offices	501
Regional offices	459
Area and zones offices	38
Field staff (in projects in countries)	483
Total	1481

The staff now includes nationals of 53 of the 88 member States, and members of most branches of the medical, public-health, and nursing professions. Many other members of these groups have worked for the Organisation in various ways during the decade. The large number of technical meetings sponsored by W.H.O. have drawn in temporarily from a number of countries many hundreds of clinicians, technical officers, scientists, and administrators. There has been almost a constant flow of short-term consultants on behalf of W.H.O. to assist a varied programme of projects in countries, and of plans and reports in headquarters and the regional offices. Such officers are not regular staff members, but leave the health services, hospitals, and universities of their own country for temporary duty with W.H.O. Some features of this type of arrangement have been discussed earlier.[1]

General Remarks

Inheriting much goodwill, experience, and resources from previous international bodies, the World Health Organisation was designed to coordinate intergovernmental health and medical work and to cooperate with other similar international agencies both governmental and non-governmental. It has proceeded far in this role. Financial support has been continuous and general. Participation of many interests, governmental and non-governmental, in its programmes has been keen, and the granting of resources to it has been generous. Countries are using both its general world-wide technical services (epidemiological, statistical, quarantine, standardisation, drugs, &c.) and its direct aid in the local development of medical and health services. It has become a comprehensive organisation with a fully developed regional system. It is now a means of associating services, institutions, and individual workers in a wide variety of medical and health programmes.

In terms of international arrangements, ten years is a short period; and no attempt has yet been made at detailed analysis and evaluation of the results of the work of W.H.O. But the growing demand for the services, as shown by the growth of its expenditure, is an index of its present popularity.

THE TENTH ANNIVERSARY

LAST Saturday the Minister of Health, Mr. DEREK WALKER-SMITH, Q.C., sent the following message to the various authorities responsible for the operation of the National Health Service in England and Wales:

Ten years ago a beginning was made with a quite new venture in the field of social welfare—the organised provision of a comprehensive health service for everybody; and today the National Health Service completes ten years' work.

They have been years not free from difficulty. There have of course been many problems—problems of new patterns of administration, problems arising out of the nation's economic circumstances, and the multifarious problems of growth and development in new directions to meet changing needs. But these ten years have been years of solid achievement, and I feel that it would be wrong to let this anniversary pass without seeking to convey to you and all engaged in the National Health Service and in the associated welfare services the sense of gratitude and appreciation so widely felt throughout the country.

We recognise most easily and acknowledge most readily our debt to the skill and care of doctor and dentist, pharmacist and optician, nurse and midwife, health visitor and home help, physiotherapist and radiographer, and all those many others who are in immediate contact with the individual person and his needs. But there are many more whose contribution may be less apparent but is no less real. I have in mind, for example, hospital domestic, kitchen, and laundry staff, maintenance workers, ambulance staff, porters, laboratory technicians, those caring for old people and for the handicapped, administrative and clerical staff, and all who, often unseen and sometimes unrecognised, by their work enable expert care to be brought more quickly and more adequately to the help of the patient.

I have also specially in mind the continuing and generous contribution, made not only by those whose daily work lies in the health and welfare services but by the thousands of men and women who render voluntary service of every kind. It is a remarkable and encouraging feature of the past ten years that the provision of comprehensive health services by public authorities out of public funds has not resulted in any falling off in voluntary work but rather in a renewal and a resurgence of it in new and varied forms. Not least remarkable and encouraging—and this is characteristic of the whole health service—has been the constant willingness of volunteers to devote their time and energies to public service as members of the authorities responsible for the local administration of the different branches of the National Health Service, thus continuing and reinforcing the tradition which has long been a distinguishing feature of administration in this country. A great and often unacknowledged debt is due to authorities like your own for their work not only in promoting the public good generally, but also in ensuring that health services shall be preserved as personal services meeting the needs of individual human beings.

Ten years is a short period in the life of these services, and we must look ahead as well as back, deriving encouragement from the success so far won to help us in meeting the changes and chances of the future. I am confident that your authority and all who are engaged in the health and welfare services will mark the tenth anniversary in this spirit, and will go forward with renewed vigour and purpose.

Public Health

ARSENIURETTED HYDROGEN POISONING IN TANK CLEANERS

A. T. DOIG
M.D. St. And., F.R.F.P.S., M.R.C.P.E., F.R.S.E., D.P.H.

ARSENIURETTED hydrogen (arsine) is an extremely toxic gas which can produce a serious illness mainly due to rapid hæmolysis. Because cases of poisoning by it are comparatively rare, many doctors are unfamiliar with its action. Therefore, despite the striking and rather characteristic syndrome, the diagnosis may easily be missed.

I call attention here to the main features of poisoning by arseniuretted hydrogen, mention the principal occupations in which the risk is present, and describe three cases which occurred in the cleaning out of acid tanks. This occupation is comparatively seldom mentioned in the literature as giving rise to cases, and is one which, though common in chemical works, is often regarded as devoid of danger.

Arseniuretted hydrogen is produced whenever nascent hydrogen comes into contact with a soluble arsenical compound. It was identified and described by Scheele in 1775. It is colourless, inflammable, and unstable, depositing arsenic on exposure to light and moisture. It decomposes on being heated to 230° C. Its vapour density is 2·68 times that of air. It is a strong reducing agent. Textbooks of chemistry describe it as having an unpleasant smell like garlic, but this cannot be relied on in concentrations met with in industry, and most victims are unaware of any unusual odour.

Occurrence and Incidence

Certain derivatives of arseniuretted hydrogen, such as lewisite (chlorovinyl-dichlorarsine), are used in chemical warfare. Apart from the manufacture of these compounds arsine is little used in industrial processes; but its evolution from dissolved arsenical material in the presence of nascent hydrogen is used as a test for minute traces of arsenic, as in the well-known Marsh's, Fleitmann's, and Gutzeit's tests.

Arsenic is a very common contaminant of metallic ores and is therefore frequently present in various commercial grades of metals, such as zinc, iron, copper, and tin. It is present in iron pyrites and so finds its way into commercial sulphuric acid made from pyrites and into hydrochloric and other acids made from sulphuric acid. The evolution of arseniuretted hydrogen may therefore be an accidental and undesired accompaniment of many industrial processes, and especially

NOTIFIED CASES OF ARSINE POISONING AND OF TOXIC JAUNDICE, 1945–56

Year	Arsine	All cases of toxic jaundice
1956	1	2
1955	—	—
1954	2	2
1953	—	—
1952	6 (2)	6 (2)
1951	2 (1)	3 (1)
1950	—	—
1949	2 (1)	2 (1)
1948	—	4 (1)
1947	—	—
1946	—	1
1945	—	6 (1)*

Numerals in parentheses indicate numbers of deaths.

* H.M. Chief Inspector of Factories in his annual Report for 1945 shows 2 deaths due to toxic jaundice in that year, but 1 of these had been previously notified in 1944.

in conditions of poor ventilation may constitute an unexpected danger. Arsenides are often present in furnace residues derived from metal smelting and purification, and the accidental wetting of these—e.g., by rain water—has caused fatal cases of arsine poisoning.

Poisoning has occurred in many industries, particularly in the smelting and refining of many metals, including gold, silver, steel, lead, zinc, tin, and aluminium, and in chemical works, as in the manufacture of acids, sulphates, and chlorides, and in galvanising, dyeing, paper manufacture, fertiliser manufacture, electroplating, and others. The manufacture of a solution of zinc chloride for use as a flux in soldering, sometimes done by workmen by the rough-and-ready method of "killing" commercial hydrochloric acid with a piece of scrap zinc, may give rise to dangerous amounts of arseniuretted hydrogen. Several professional chemists have been affected in the course of their laboratory work. Dimethylarsine is well known as having been the cause of many fatal cases of poisoning in residents of damp houses; it was liberated from Scheele's green, a wallpaper pigment no longer used as such in this country, by the action of a mould.

It seems likely that most cases which are recognised are notified to the Factory Inspectorate, because, apart from certain research departments and laboratories not under the Factories Acts, exposure to arsine would most often take place on factory premises. Cases are usually notified either as "toxic jaundice" or as gassing accidents, but they could conceivably be notified as toxic anæmia or even as arsenical poisoning. During the twelve years 1945–56 13 cases, 4 of them fatal, of poisoning by arseniuretted hydrogen came to the notice of the British Factory Department (H.M. Chief Inspector of Factories 1945–56). The accompanying table shows the distribution by years and, for comparison, the total number of notified cases of toxic jaundice due to all causes, including arseniuretted hydrogen.

This table brings out the important role of arseniuretted hydrogen in causing toxic jaundice in peacetime, because if we exclude 1945 (when all 6 cases were due to trinitrotoluene), 13 of 20 cases were due to arseniuretted hydrogen in 1946–56, and 13 out of 15 cases in 1949–56. The causes of the 26 cases of toxic jaundice were as follows:

Arseniuretted hydrogen	13 (4)
Trinitrotoluene	6 (1)
Carbon tetrachloride	2
Chlorinated naphthalene	1
Paint-remover	1 (1)
Other	3

Numerals in parentheses indicate numbers of deaths.

The occupations of the 13 persons who were poisoned by arseniuretted hydrogen were as follows:

Tin smelting; handling arsenical dross	6 (2)
Cleaning sulphuric acid tanks	3 (1)
Laboratory workers	2
Cleaning reaction in vessel which had contained arsenic acid	1(1)
Mixing oxalic acid and other chemicals in vessel contaminated with As_2O_3	1

Numerals in parentheses indicate numbers of deaths.

The 13 cases occurred in seven incidents, all 6 tin-smelters being affected in one and both laboratory workers in another. An excellent account of the 6 cases in the tin-smelters is given by Macaulay and Stanley (1956).

Symptoms and Diagnosis

Arseniuretted hydrogen is one of the most toxic gases known. Concentrations of 3–10 p.p.m. will produce slight symptoms after several hours' exposure, and concentrations of 16–30 p.p.m. are dangerous after $^1/_2$–1 hour. The maximum allowable concentration recommended by the International Labour Office for an 8-hour working day and the "threshold limit value" adopted by the American Conference of Governmental Industrial Hygienists, 1957, are 0·05 p.p.m. (compared, for example, with 100 p.p.m. for carbon monoxide). Repeated exposure to low concentrations may have a cumulative effect.

Two simple chemical tests are available for detecting small concentrations of arseniuretted hydrogen, one using silver-nitrate papers and the other mercuric-chloride papers. The Department of Scientific and Industrial Research (1940) describes a quantitative test.

After exposure to toxic concentrations of arseniuretted hydrogen there is usually a delay of 2–24 hours before the onset of symptoms. When arseniuretted hydrogen enters the blood-stream it combines with the hæmoglobin and hæmolyses the red blood-cells. The first symptoms are usually vague malaise, nausea, giddiness, and headache, rapidly progressing to severe illness with vomiting, intense headache, pains in the loins, and the passage of dark urine (hæmoglobinuria). The progress of hæmolysis rapidly causes profound anæmia. The liver and kidney functions are severely disturbed and usually break down in the effort to eliminate the products of the disintegrated corpuscles. Jaundice is usually evident on the 2nd or 3rd day and increases to an intense coppery hue. There is oliguria with albumin, casts, hæmoglobin, and methæmoglobin, and in severe cases there is suppression of urine. Œdema of the lungs, with accompanying cyanosis, is a common complication, and in fatal cases there is usually delirium followed by coma.

It will be appreciated from this description and the three illustrative case-reports below that a sudden onset of severe illness with gastric upset and the passage of urine the colour of port-wine in an industrial worker or chemist is sufficient to direct suspicion to the possibility of poisoning by arseniuretted hydrogen. Rapidly developing jaundice, anæmia, and evidence of kidney damage greatly strengthen the suspicion. Inquiry should be made about the patient's occupation, particularly the precise work on which he was engaged during the previous 24 or 36 hours. The whole working-time should be accounted for because exposure may have been limited to a few minutes. The diagnosis is clinched by obtaining a history of exposure or by finding arsenic in the urine, because during the acute stage and for some weeks afterwards arsenic is excreted by the kidneys.

In making a retrospective diagnosis after recovery in patients where the correct ætiology was missed during the acute stage, examination of the hair and nails may reveal arsenic. In this connection the method of activation analysis of tissues described by Dewar and Lenihan (1956) deserves mention. This very sensitive method depends on the induction and subsequent measurement of radioactivity in the sample by treatment in a nuclear reactor. It enables very small amounts of tissue to be

analysed, and abnormal amounts of arsenic may be found in a single hair.

Prognosis and Treatment

Prognosis turns largely on the state of the kidneys and is generally related to the amount of urine passed: the smaller the amount the graver is the case. Death usually takes place between the 4th and 10th days. Kober and Hayhurst (1924) give the fatality-rate of recorded cases as 25–30%. They suggest that this may be artificially high because fatal cases tend to be recorded more than recoveries. Locket et al. (1952) cite mortality-rates of 20–31%. Hunter (1955) refers to 7 deaths in 25 cases (28%) in tin-refining. In the 13 cases referred to above it is 31%.

The danger being usually intermittent and fortuitous, the patient is rarely actually exposed to the gas when symptoms develop. If he becomes ill while at work he must immediately be withdrawn from exposure, and any contaminated clothing must be removed. Early removal of the patient to hospital is essential, and general measures should be instituted forthwith to deal with pain and anxiety and to minimise shock. Early deaths are often due to pulmonary œdema. When this is present, oxygen, preferably under pressure, probably offers most hope of averting death.

High hopes that dimercaprol would prove of value have not been sustained; it has been used in most of the recently published cases, but the results have been far from convincing, even when the dosage was adequate. Locket et al. (1952) say that, although it is of doubtful value, dimercaprol should be given if the patient is seen within the first 24 hours; after that it is more likely to add to his burden.

Dextrose and saline solution given intravenously with calcium gluconate has been advocated, but the daily fluid intake must be kept low in anuria and severe oliguria and the volume and composition of the body fluids as nearly normal as possible. Hyperpotassæmia must be guarded against.

Most workers advocate transfusion, preferably with packed cells, but Locket et al. say a transfusion should only be given if there is severe anæmia. McKinstry and Hickes (1957) say that if they see a patient with symptoms of severe poisoning, they intend to begin massive exchange transfusion as soon as the diagnosis is made, thereby helping to reduce the amount of arsenic and arsenical compounds in the blood and to get rid of reduced hæmoglobin and cellular debris and so to lessen or to prevent the blockage of the renal tubules.

Cases in Tank Cleaners

The three cases briefly described here occurred at different times in different chemical works; but all were in men who had entered tanks, which had contained sulphuric acid, to clean them. All the tanks had held acid made from iron pyrites—in two cases exclusively; in the third, a tank used for transport of acid by rail, oleum (fuming sulphuric acid), made by burning sulphur, had also been carried occasionally.

The arsenic content of sulphuric acid made from pyrites varies a good deal but, calculated as As_2O_3, is usually about 0·2–0·3% and may sometimes be more. Glaister (1908) cites arsenic contents of commercial sulphuric acid up to 0·45% and for hydrochloric acid as much as 0·691%. Since the tanks were lined with lead, it was expected that the deposit would be almost entirely composed of lead sulphate. Analysis of part of the deposit concerned in case 2 below, however, showed that it contained 45·0% by weight of As_2O_3, and a later sample from another tank contained 18·6%. It seems that the arsenic impurities in sulphuric acid tend to settle out on standing. Glaister (1908) quotes Cameron as having reported in 1856 that about 1 oz. of crystallised arsenious acid was deposited after long standing from 8 lb. of sulphuric acid.

When the deposit is not very hard it can be removed by directing a strong jet of water on to it from outside the tank. When it is hard, the tank has to be entered and the deposit removed by hand with such tools as a scraper and a shovel. Cleaning may be required at intervals of 6–12 months, and the method of hosing, followed if necessary by entry, has been used for years. Chemists, managers, and workmen do not appear to have anticipated the presence of any dangerous gas; and no special precautions, such as the use of breathing-apparatus, have in the past been taken in the three factories concerned. Suitable protective clothing was, of course, provided and worn. According to the size of the tank whether it contained internal baffle plates or not, the hardness of the deposit, and other factors, the cleaning of one tank might take a few hours or a few days.

Case 1.—A man, aged 52, was certified as having died of hæmolytic anæmia. Death was not definitely attributed to occupation, and no suggestion was made that arsine might have been the cause. The occurrence came to my notice several months after death, and on inquiry the typical story of poisoning due to arseniuretted hydrogen came to light.

Exposure and onset.—The man had been employed for some years at a factory where sulphuric acid was manufactured from iron pyrites by the chamber process. On a Saturday morning he entered a stock tank, which had contained concentrated sulphuric acid, to clean it. He was in the tank for about half a hour, from 8.30 to 9 A.M. He finished his shift as usual at noon and went home. He became ill about 5.30 P.M. on that day with colic, abdominal pain, and vomiting. Next day he was admitted to hospital, where he died on the 6th day of the illness.

On admission he was much jaundiced and anuric. 2 oz. of urine the colour of port-wine was obtained on each of the following 2 days, and thereafter he was anuric until death. His urine contained hæmoglobin and methæmoglobin. His blood hæmoglobin was 81% on admission but on the day preceding death had decreased to 45% and the red cells to 2,760,000 per c.mm. No hæmolysins were found in his blood. Treatment was by intravenous drip with glucose.

Necropsy findings.—The lungs showed severe hæmorrhagic œdema, with many hæmosiderin-laden phagocytes in the alveoli. The liver was slightly enlarged, rather pale, and soft, but without fatty degeneration or necrosis; the centres of its lobules showed a good deal of pyknosis of the liver-cells. The kidneys showed severe hæmoglobinuric nephrosis, almost all the collecting tubules containing precipitated hæmoglobin or acid hæmatin. The loops of Henle and the distal convoluted tubules contained many casts. The glomeruli were practically normal. The cause of death was acute hæmolytic anæmia and renal failure.

Case 2.—A man, aged 44, had been a chemical-works labourer for more than 5 years and had cleaned many acid tanks in that time. Before his illness he and his usual mate had been engaged in cleaning a rail-car tank which had been used for many years for transporting sulphuric acid. It was 15 ft. long by 5 ft. in diameter, and had one man-hole; the interior was divided into three compartments by two baffle-plates, each with a man-hole. The tank had usually carried concentrated pyrites acid but in recent months had contained oleum at times. The deposit was very hard and could not be dislodged after flooding and hosing. The men took it in turns

to enter the tank for spells of about ½ hour each. On the Friday, when work started, and on the following Monday each man probably spent 2–2½ hours inside the tank, on the Saturday morning about 1 hour each, and on the Tuesday about 1½ hours each before noon, when the work was completed. About 2½ tons of deposit was removed. The mate was unaffected; but the patient became ill early on Tuesday evening with nausea, abdominal pain, and headache, which later became severe and were accompanied by vomiting.

On admission to hospital next morning he had hæmoglobinuria and was icteric. Examination of his blood showed hæmoglobin 80%, red cells 4,400,000 per c.mm., and white cells 14,000 per c.mm. Serological tests for Weil's disease were negative. The man made an excellent recovery without any specific treatment, and no transfusions were required.

Laboratory tests.—Analysis of two types of pyrites acid which had been carried in this tank car showed an arsenic content, expressed as total As, of 0·27% and 0·36%. The arsenic content of a sample of oleum was 0·01%. The men had used a steel scraper, an iron shovel, and a galvanised iron bucket in the tank. Laboratory tests with the deposit showed that arseniuretted hydrogen was generated from it by using zinc, and traces by using mild steel. A quantitative analysis of part of the deposit removed last during cleaning showed the astonishing figure of 45·0% arsenic calculated as As_2O_3.

Case 3.—A man, aged 35, was notified as having toxic jaundice of unknown origin, the notification being received after his recovery. Though it was suspected that his illness might have had an occupational cause, the possibility that this might be arseniuretted hydrogen had not been considered, and the mangement and staff of the factory were unaware that this hazard existed in the works.

Exposure and onset.—On the day his illness started, the patient had entered an acid-storage tank to clean it. The tank measured 6 ft. high by 9 ft. in diameter and had held concentrated oil of vitriol (98% sulphuric acid) made from pyrites. After washing out the tank several times with a hose he had entered it, taking a copper shovel and a galvanised pail with him. He spent two or three periods of ½ hour each in the tank. When he returned home in the evening he felt tired and was unusually thirsty but had no appetite. Severe headache developed, and during the night he vomited and passed urine which he described as nearly black.

On admission to hospital next day he was extremely ill and jaundiced, and his urine contained methæmoglobin and albumin. Liver-function tests showed some liver damage.

Treatment and progress.—He was treated with intravenous methylene-blue and ascorbic acid and with cortisone 200 mg. daily during the acute stage. In addition he had a high-carbohydrate low-fat diet. He made a full recovery. His hæmoglobin decreased to 40% but at the time of discharge was 95%. Normal liver and kidney functions were entirely regained, and 2 weeks after his discharge his serum-bilirubin was 0·4 mg. per 100 ml., his hæmoglobin was 100%, his urine was normal except for excess urobilinogen, and he looked and felt well.

Laboratory tests.—Specimens of his hair and nails were obtained 10 weeks after the onset and subjected to analysis for arsenic content by the activation technique. The specimen of hair was reported as containing 7·6 p.p.m. of arsenic and the nails 4 p.p.m., both values being rather high. The tests, repeated after 4 months, showed the arsenic content of the hair as 1·5 p.p.m., which is within normal limits, but the content of the nails was still rather high at 6 p.p.m.

Prevention

Undoubtedly the most important factor in prevention is a knowledge of the risk. The three cases described occurred because the danger was not appreciated, and it seems incomprehensible that the managements of the three factories did not foresee the risk of generation of arseniuretted hydrogen during the work of cleaning the tanks. The cases occurred in 1949, 1951, and 1956, and obviously there had been little or no interchange of information between the factories nor effective publication in the chemical trade journals, and the references to the cases in the annual reports of H.M. Chief Inspector of Factories had been missed. It is to be hoped that a knowledge of this serious danger will soon permeate to the staffs of all factories where acid tanks may have to be cleaned, and from them to the workmen who have to do the job.

So far as possible, acid tanks should be cleaned without entry. When the deposit is soft, this can usually be done by repeatedly flushing with water and draining. When the deposit is hard, softening might be effected by strong alkalis or by steam. According to the nature and construction of the tank, in some cases it might be possible to bore or cut a hole or holes in the bottom or sides to allow of the insertion and manipulation of scraping tools. When the tanks are entirely composed of sheet lead, this would not offer much difficulty. It might be possible to prevent the deposit from becoming very hard by arranging for regular cleaning at relatively short intervals.

Proper equipment for the job should include protective clothing consisting of acid-resisting suits, head covering, and rubber boots and gloves, and non-metallic tools, such as scrapers, shovels, and buckets. Breathing-apparatus should be worn if entry is necessary, the most convenient type probably being an air-line mask enabling the worker to breathe fresh air through a flexible hose extending to the open air outside the tank. A mate should always be immediately at hand outside; and, where the entrance to the tank is small, or where there are interior baffle-plates which might hamper rescue in an emergency, it is probably wise for the worker entering to wear a safety belt, the attached rope being held by his mate outside.

Legal requirements are quite definite about precautions which have to be taken when work is done inside enclosed spaces where dangerous fumes are liable to be present. They are laid down in section 27 of the Factories Act, 1937, modified by section 11(2) of the Act of 1948. In factories to which the Chemical Works Regulations, 1922, apply Regulations 6–9 are particularly relevant to the work in question and must be observed.

Discussion

Poisoning by arseniuretted hydrogen produces a serious illness with a striking clinical picture. The dominant features are acute hæmolysis and jaundice, and perfectly correct diagnoses, such as acute hæmolytic anæmia, hæmolytic jaundice, and toxic jaundice, are easily made on the clinical findings. The true ætiology, however, is often overlooked. In two of the three cases described (cases 1 and 3) the possibility that arseniuretted hydrogen might be the cause does not appear to have been considered until investigations were made some time after the illnesses, although certainly in case 3 an industrial cause was suspected. Case 2 was correctly diagnosed by the general practitioner as arsine poisoning; he had, by an extraordinary coincidence, attended case 1 about 18 months previously and instantly recognised the typical syndrome.

The reason why the ætiology is missed is of course the rarity of the condition. Very few physicians in general or in hospital practice ever have an opportunity of seeing a case. It should, however, be noted that arseniuretted hydrogen is one of the commonest causes of industrial

toxic jaundice in peacetime, when trinitrotoluene is not being manufactured on a large scale.

The ignorance of chemists and plant managers about this grave risk seems to me much more remarkable. It is a well-known fact that acid made from pyrites contains arsenic as an impurity, and the presence of arsenical compounds in the deposit in tanks which have contained commercial sulphuric or hydrochloric acids should be appreciated and the danger of evolution of arsine recognised. In none of the three factories concerned with these cases was entry into acid tanks for cleaning considered to carry any risk of exposure to dangerous gases, and such entry had taken place on several occasions without special precautions having been taken. So far as is known, no harmful effects had followed these previous entries. Even after the occurrence of cases 1 and 3 the managements and technical staffs were unable to pinpoint the hazard. At the factory where case 2 occurred, however, the origin of the gas was recognised when the correct diagnosis of poisoning by arseniuretted hydrogen was known, and the works chemist demonstrated its evolution from the deposit from the tank with iron and zinc, the metals of the shovel and galvanised bucket used.

It is quite probable that unrecognised cases of arsine poisoning have occurred in the past from the cleaning of acid tanks when less thought was given to possible occupational causes of illness than today. The extreme toxicity of the gas makes it essential that works managers, chemists, and foremen in factories where sulphuric acid is stored in tanks should show a much greater awareness of this grave danger than they have shown in the past.

It seems too that a reminder to the medical profession would not be out of place, for, although poisoning with the gas usually produces a very characteristic syndrome, it is one which few physicians have an opportunity of seeing, and the diagnosis, or at least the ætiology, is thus easily missed.

It is worth emphasising too that H.M. Factory Inspector should be notified immediately the cause of the illness is ascertained or, even better, as soon as an industrial cause is suspected. If this were done, an immediate investigation would be made at the factory. Since the cleaning of one tank may take several days, as in case 2, early notification—for example by telephone—of one case may lead to the institution of suitable preventive measures before a second case results. H.M. Medical Inspectors of Factories will be ready to give assistance in regard to diagnosis and investigation.

Summary

Poisoning by arseniuretted hydrogen, though relatively rare, is one of the commonest causes of toxic jaundice in peacetime. In spite of the typical syndrome cases may be missed.

The risk of poisoning by arseniuretted hydrogen in cleaning tanks which have been used for storing or transporting strong acids does not appear to be fully appreciated. Three cases arising from cleaning sulphuric-acid tanks are described, one of them fatal.

This danger should be made widely known among technical staff of factories where strong acids are stored. Doctors and factory managers should realise the importance of early notification of cases to the Factory Inspectorate.

I received a great deal of help and information from managers, chemists, and other staff of the factories where the three cases occurred and from general and hospital practitioners who attended the affected men. I thank them all, and Dr. Colin Campbell for information about the necropsy findings in case 1, and Dr. J. M. A. Lenihan for the activation analyses on material from case 3.

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Infectious Diseases in England and Wales

Disease	Week ended June			
	7	14	21	28*
Diphtheria	2	—	—	5
Dysentery	883	893	838	873
Encephalitis:				
Infective	3	4	2	2
Post-infectious	1	10	1	1
Food-poisoning	184	275	279	261
Measles, excluding rubella	6433	5594	6108	6026
Meningococcal infection	20	15	16	22
Ophthalmia neonatorum	40	29	14	27
Paratyphoid fever	6	2	4	8
Pneumonia, primary or influenzal	265	247	214	218
Poliomyelitis:				
Paralytic	16	20	22	29
Non-paralytic	15	9	14	14
Puerperal pyrexia	203	200	223	170
Scarlet fever	615	666	659	662
Smallpox	—	—	—	—
Tuberculosis:				
Respiratory	571	560	555	565
Meninges and C.N.S.	8	5	8	7
Other	90	104	91	80
Typhoid fever	7	8	4	1
Whooping-cough	641	747	800	783

* Not including late returns.

Points of View

EVOLUTION AND ILLNESS*

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". . . What do these rudiments, these apparent imperfections mean? There must be some cause for them; they must be the necessary results of some great natural law."—A. R. WALLACE (1855).

" It is a relief to have some feasible explanation of the various facts, which can be given up as soon as any better hypothesis is found."—CHARLES DARWIN to A. R. WALLACE (1868).

A FRESH field of clinical investigation opened when it was recognised that certain primary disturbances of the human mind can damage distant and diverse structures throughout the body. Doctors working within the complex environment of modern society are re-examining some aspects of disease that they believe to be related to such factors as the growing complexity of life and the closer impact of parents on their smaller families. There is a desire to contain the vagaries of stress-conditioned illness within the bounds of a rational physiology, and an increasing recognition that the anatomical distribution of the consequent organ damage is often influenced by the genetic constitution of the patient, of his family, and of his race.

In the wild state of Nature, we understand something of the basic laws of selection acting on gene-conditioned variations in plants and animals. In agricultural and horticultural selection we see at work the minds of men,

* The text of the essay from which this article has been condensed can be obtained from the author.

seeking to improve their stock by the conscious application of skilled experience. In man, since he became human, unique forces, still largely veiled in mystery, have acted to condition his fitness for selection, and to produce, partly by the greater relative safety of a civilised environment, certain modifications of behaviour and of structure. Yet all this great advance has been achieved with the maintenance of—and (some believe) partly because of—the very generalised human anatomical form. Man reveals an " astonishing conservatism of anatomical structures as the result of which their traces may still be detected millions of years after they have ceased to have any function " (Le Gros Clark 1950).

Commonly found on human skin are structures which, judging by their anatomy and histology, are significant ancestral characters dating to man's early mammalian and amphibian-reptilian evolution. In the past a study of these structures, which were regarded merely as " beauty-spots " or " birthmarks ", would have seemed irrelevant to clinical medicine. But their identification as evolutionary vestiges (de Cholnoky 1939, Laidlaw and Murray 1933, Stout 1948) adds a new interest to the study of the supernumerary nipple and the pigmented moles and other nævi, especially since workers in human genetics (McKusick 1956) have demonstrated, in such diseases as the Marfan syndrome, a close genetic linkage between superficially trivial anatomical characters and grave hereditary diseases.

OBSOLETE DEFENCE MECHANISMS

The suggestion that obsolete defence mechanisms from very remote dates in human evolution can be reactivated under the influence of emotional stress or long-continued anxiety (Harper 1953) seems less improbable in the light both of the clinical facts and of the collateral evidence deriving from the influence of pædomorphism in the recent development of the human brain. This concept—that in certain highly progressive species, including man, evolutionary advance has been achieved by retention in the adult organism of structures formerly found only in the fœtal stages of the species—was first given the name of " pædomorphosis " by Garstang (1922). Hardy (1954) emphasises the close identity of Garstang's theory with Bolk's (1926) thesis of " fœtalisation " especially of the human skin. de Beer (1951) wrote: " It must not be pretended, of course, that pædomorphosis itself can account for the essential character of man—his mental capacities; we may, however, say these could not have been evolved without pædomorphosis ". The clinician who appreciates the profound anatomical significance of a pædomorphic element in modern human evolution may properly inquire into the possible impact of such a phenomenon on the physiology and diseases of contemporary man. Should it prove true that anatomical characters of fœtal type have been significantly retained in the human adult, a hypothesis that certain illnesses are based upon " morbid echoes " of archaic defence reflex patterns deserves careful examination.

In relating human illness to reflex defence patterns, three groups of possible physiological mechanisms might be considered.

Group 1.—Those reflex patterns that are present and are still used for their physiological purpose in man. Under certain adverse conditions of the environment, I suggest, a close association may exist between the reflex defence mechanism and a grave pathological process. In this connection I shall refer with frank but necessary oversimplification, to the ætiology of phlebothrombosis.

Group 2.—Here no physiological service is immediately obvious at human level, but the clinical course of certain diseases suggests that they may be associated with obsolete reflex defence patterns of vital importance in the mammalian forebears of man. Peptic ulcer can be an illustration here.

Group 3.—These reflex patterns are so archaic that it might seem absurd to suggest that human illness could be related to them. Yet I believe that this will be shown to be true. Proof of the existence on human skin of common structures relating man to the amphibian-reptilian era of his evolution will encourage the further investigation of what may prove to be an important new aspect of disease. As illustrations, I shall mention, with diagrammatic oversimplification, three illnesses: allergy, diabetes, and certain neoplastic states.

Group 1

Every physician who has practised in the wards of hospitals where acute cases are nursed must have been puzzled by the frequency with which excellent work meets the unexpected and often grave complication of pulmonary embolism, due to detachment of a clot which has formed in the veins. In relation to my hypothesis, the significance of this group of illnesses lies in the laboratory evidence that, in the lower mammalia and in man, blood tends to coagulate more quickly when danger threatens. Stoker (1945, 1952) has demonstrated a considerable reduction in the clotting-time of rabbits after an incident causing them fear. A similar reaction has been demonstrated by him in human beings under emotional stress. Hunter et al. (1941), in 351 unselected consecutive necropsies, examined the calf muscles macroscopically and microscopically and found antemortem clots (often bilateral) in rather over half of them.

Deferring to most contemporary opinion, the clinician, losing his patient from massive pulmonary embolism consequent on phlebothrombosis, attributes the tragedy to rest in bed, to a fall in blood-pressure, or to debility. But observation over many years has convinced me that fear, or lack of confidence by the sensitive patient, has sometimes played a significant part. Doctors, nurses, and administrators should be taught these physiological and clinical possibilities and recognise their implications. Though nervous patients often find security in the wards of a hospital, and are relieved of some of the morbid potential of their anxiety in this environment, others react unfavourably to the often little-concealed events of the general ward. It may well be that some of the cases of phlebothrombosis attributed to the uncomfortable seats in air-raid shelters were associated with this shortening of the clotting-time in the presence of fear.

Here, then, is one example of an illness whose precipitating cause may be the morbid echo of a physiological process. This particular process, we may suppose, was originally evolved, perfected, and selected because it prevented blood-loss in battle or in flight and so conserved the integrity of the blood-volume for escape or victory.

Group 2

Harvey Cushing (1932) drew attention to the enormous literature, the vast number of theories, and the conflicting evidence surrounding the local lesion in peptic ulceration. He expressed his opinion that, whatever the exact mechanism causing the local lesion might be, it was in the nervous system of man that the true causation of this illness would be discovered. It is increasingly accepted that in the modern prefrontal areas of the human brain are centres closely linked with the age-old autonomic system. Brandt (1922) suggested that the parasympathetic antedates all other nervous structures in phylogeny, except

the very early endocrine system. Should pædomorphosis be proved to have conditioned man's recent evolution, apparent inconsistencies may be better understood, and the possibility that this type of illness may be based upon an obsolete physiology may be established as a fact. In a feeding animal faced with an emergency in which a maximal supply of blood to the skeletal muscular system was required, we may discern a reflex mechanism that, by violent closure of the pylorus and the act of vomiting, halted digestion. When fear and anxiety produce a morbid dynamic of tension in the human brain, some echo of this reflex may, I believe, be producing the organ dysfunction and damage.

Group 3

Let us now briefly examine the distant end of the time scale, the amphibian-reptilian epoch of human evolution. Elsewhere I have described manifestations of allergy as possibly based on the integrated oxygenating reflexes of skin, lungs, and gills—a normal physiological mechanism in the distant amphibian era (Harper 1948, 1951, 1953, 1955). I believe it is but the logical application of a true hypothesis to seek for other illnesses in this third group of reflex defence patterns, in view of the unique, yet very common, reptilian structures demonstrated on human skin by Laidlaw and Murray (1933) in their classical work on pigmented moles and their relationship to the evolution of the hair follicles in man.

Long before the discovery of insulin, Osler (1892) wrote of diabetes mellitus: "Mental shock, severe nervous strain, and worry precede many cases". Twenty-five years' experience in directing a diabetic clinic have convinced me that this mysterious and highly complex illness will be recognised, in some of its forms, as a disease of stress. It is perhaps significant that the islet tissue of the pancreas retains its own autonomic nerve-supply, that to the beta cells being especially heavily innervated by the age-old parasympathetic system, so closely connected in the distant past with archaic reflex patterns of defence.

Is it possible that the future may reveal knowledge that will justify another unexpected, yet I suggest logical, extension of the hypothesis, and bring within its scope as "morbid echoes" of this third group of reflexes certain types of malignant cell-growth? Remarkable regeneration of entire limbs after damage was a commonplace event in the amphibian-reptilian epoch of man's evolution. The nature of the physiological forces at work in the organism while such extensive injury was being repaired is still unknown. The process of such massive yet orderly repair can still be watched in the axolotl, that remarkable example of neoteny (extension of the larval stage), where mature reproduction occurs in the larval form of the amphibian *Amblystoma tigrinum*. We cannot at present comprehend these physiological mechanisms even in such lowly organisms. I believe, however, that in the reactions of man's body to certain exogenous and endogenous carcinogenic stimuli we may yet find that we are witnessing the results of a distorted and destructive physiology of archaic origin that formerly furthered active yet purposeful cell-growth after injury. The influence of anxiety and mental shock on the course of a malignant illness has become increasingly apparent to clinicians (Ogilvie 1957).

CONCLUSION

The theory of evolution has become one of the great cosmic generalisations, and in whatsoever sphere it has been wisely applied it has enlightened what before had been an ill-defined field of human experience. The time is ripe for its logical and bold application to clinical medicine.

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Congresses

GYNÆCOLOGY AND OBSTETRICS

AT the second world congress of the International Federation of Gynæcology and Obstetrics, held in Montreal on June 22–28, 61 nations were represented.

Canada's Problems

Mr. WALDO J. MONTEITH, Canadian Minister of National Health and Welfare, remarked that Canada is the third largest country in the world, occupying $3^1/_2$ million square miles, with a small population of 17 million largely based on a 200-mile strip across the country's southern border. There is disparity of progress because Canada has been settled in waves, first Quebec, then Ontario, and the west some hundred years later; only now is the north being settled.

Disordered Uterine Activity

Professor BELOSHAPKO (U.S.S.R.) said that the idea of regulating the character of labour was generally accepted, and he drew attention to the vagaries of uterine action mentioning precipitate labour and inertia. Inertia he believed to be the more important. Having stated that the aim in uterine inertia was to reduce the necessity for operative procedures, he described many methods of stimulating uterine contractions. In his summary of prophylaxis and treatment he stressed psychoprophylaxis; exercises, massage, and ultraviolet radiation; and the correction of sleeplessness by having special sleeping-rooms and by the careful organisation of the leisure especially of long-stay patients. He believes in adequate feeding and in not putting the woman to bed too soon in her labour.

The Hypothalamus

Prof. G. W. HARRIS (Britain) described very clearly the careful experiments by which the relationships between hypothalamus, pituitary, reproductive organs, and breasts were established. Impulses from the hypothalamus reach the anterior lobe of the pituitary gland by way of the vascular portal system, as has been shown by transplanting the pituitary gland first into the capsule of the kidney, when its hormone activity ceased, and then returning it to its original site, where the portal circulation was reestablished and pituitary function restored. Not only has the hypothalamus a depressant action on the adenohypophysis but also there is a stimulating action. Follicle-

stimulating hormone may be released under the stimulation of tumour, and Professor Harris suggested that precocious puberty resulting from hypothalamic lesions may be explained in this way.

The humoral interplay between hypothalamus and adenohypophysis is clearly established by the absence of any effect if the pituitary is stimulated electrically, in contrast to the marked effect if the hypothalamus is given a similar stimulation.

The relationship between hypothalamus and neurohypophysis is by contrast a nervous one. Stimulation of the hypothalamus leads to the production by the neurohypophysis of oxytocin, which in turn causes pregnant uterine muscles to contract and also causes the ejaculation of milk from the breast by its action on the contractile tissue in the mammary gland.

The precise routes by which afferent stimuli reach the hypothalamus are not clear, probably because they are so varied. This whole study accords with the known effect of emotional and other environmental stimuli on both uterine action in labour and successful lactation. It may now be said that the precise way in which fear and other harmful stimuli affect parturition and lactation is well on the way to being worked out.

Amniotic Membrane

Professor BAUTZMANN (Germany) gave a fascinating account of the muscular activity of the amniotic wall in the chick embryo and compared this with the absence of any corresponding muscular activity in higher mammals. He expressed the opinion that the rhythmic activity of the amniotic membrane, which was illustrated by film, had the important effect of moving the nutrient material around the chick, and he showed conclusively that this movement was independent of fœtal activity.

Fertilised Ovum

Dr. BRADLEY PATTEN (U.S.A.) said that the fertilised ovum develops a thick wall around it, and this has two purposes: (1) it acts as a barrier to the entry of other spermatozoa, and (2) it prevents the enlargement of the fertilised egg during the early days of division and subdivision and so keeps it small enough to pass through the fallopian tube. Apparently, too, this cluster of cells with its thick envelope is particularly sticky opposite the inner cell mass and this facilitates implantation. Dr. Patten described and illustrated the development of the fœtal circulation. He showed how the primitive tubular heart begins to contract before any connection has been made with the primitive blood-vessels, and illustrated the early formation of blood-cells and the coalescing of primitive blood-vessels.

Sex Chromatin

Prof. MURRAY L. BARR (Canada) spoke briefly about the three methods of examination for female sex chromatin—by mucosal smear, skin biopsy, and blood film. He drew attention to the occasional flattening out of the chromocentre as a source of error. The two main groups of disordered sexual development comprise those exhibiting partial masculinisation and those exhibiting intersex.

It is important to distinguish the adrenogenital syndrome from male pseudohermaphroditism so that cortisone may be started without delay and the severe metabolic crises characteristic of the untreated adrenogenital syndrome prevented. He also drew attention to the possible virilising effect on female infants when the mother is treated with progesterone during her pregnancy.

Turning next to gonadal dysgenesis, he pointed to its relationship with coarctation of the aorta. The ætiology is not known.

In male pseudohermaphroditism there is deficient interstitial-cell development with a consequent trend towards femininity in development.

The testicular feminising syndrome usually associated with the name of Kleinefelter presents the unusual combination of testes, absent uterus, female external genitalia, and normal female stature. There is failure of masculinisation of the external genitalia and clumping of the Leydig cells. Half of these cases are sex-chromatin-positive and half negative.

Exceptionally some sperinatogenesis has been noted even in sex-chromatin-positive cases. Professor Barr drew attention to the greater frequency of this syndrome in mental defectives and put forward a plea for a closer study of these cases, believing that such a study might lead to some understanding of the causes of mental deficiency —a subject which he maintained had been much neglected by medical research-workers.

Uterine Contraction

Dr. ROBERTO CALDEYRO-BARCIA (Uruguay) reviewed the investigations carried out by the team in Montevideo on uterine contractility by the simultaneous recording of the pressures in different parts of the uterus under different conditions. He also presented new work based on the continuous recording of amniotic-fluid pressures in labour. He defined uterine intensity of contractions as the difference between the resting and contracting uterine pressures, the frequency of contractions as the number per ten minutes, and the uterine activity as the product of the intensity and frequency; uterine activity is expressed in Montevideo units.

As pregnancy advances there is steadily increasing uterine activity until at the onset of labour this amounts to about 100 Montevideo units: by the second stage the activity has increased to 250 Montevideo units. Distension of the cervix leads to nervous impulses reaching the hypothalamus and then the posterior pituitary with consequent release of oxytocin and augmented uterine action.

The simultaneous recording of myometrial activity by microballoons placed in various parts of the uterus has shown up the difference between the normal and abnormal patterns. Though the acme of the contractions is reached normally by all parts of the myometrium at the same time, the onset of the contraction starts at the cornu and spreads from here throughout the uterus. The pain of labour is caused by cervical distension and later perineal distension. Much work on abnormal action was described. Hypoactivity of the uterus only led to 40 Montevideo units, and this is not enough to cause labour to progress. In such cases a continuous oxytocin drip is used, and the fluid is given with great accuracy by means of an infusion pump.

Adrenaline first inhibits uterine activity, and then there is a rebound phenomenon with increased activity. Pethidine and morphine have no effect on uterine action. Toxæmia is usually associated with good uterine activity. Spinal anæsthesia has no effect on normal uterine activity; but if the resting tone of the uterus is high, perhaps because of fear, then it can be beneficial. The dorsal position leads to better muscular activity than the lateral positions.

Placental abruption raises the tone and no drug has

so far been found to lower this; artificial membrane rupture is the best treatment, but it does not lower the tone.

If hydramnios with high resting tone is treated by membrane rupture, the tone is lowered and labour is likely to ensue: in contrast hydramnios with an initial low tone may be tapped without such a likelihood of labour starting.

Dr. Caldeyro-Barcia then went on to describe the qualitative faults in uterine action, showing tracings of irregular contractions. Several centres of contraction, acting independently, can each have the effect of inhibiting and largely neutralising each other's actions. In some cases, at least, intravenous oxytocin in carefully controlled quantity has been found to have a striking coordinating effect. Spinal anæsthesia had a similar effect, as did hypnosis.

Probably fear and other harmful stimuli adversely influence uterine action by way of the adrenals and by the release of adrenaline and noradrenaline.

Parliament

Ten Hospital Years

As " chairman of Parliament's own hospital ", Lord NATHAN appropriately opened the debate in the House of Lords on July 2 on our hospitals and their progress during the past ten years. The time was, he thought, suitable for such a review, for the start of the National Health Service had in many ways marked a revolution in the social life and habits of the country. It had affected vast numbers of the population, and it had influenced the standing and procedures of the medical, dental, and nursing professions. It was, perhaps, the central feature of the Welfare State. The hospitals were an important part of the service, and he thought that the Ministry of Health and the doctors, nurses, and administrators should be congratulated on the adaptability, assiduity and devotion they had shown in running the hospitals in the unfamiliar circumstances of the last ten years. He admitted that he was surprised, though delighted, by the amount of voluntary service still offered. At the Westminster Hospital the number of volunteers was greater than ever, which showed that people would not consent to being deprived of the opportunity for service.

BRICKS AND MEN

Turning to finance, Lord Nathan said that it had been a period when " I would " had had to wait upon " I can ", and he was uneasy lest capital expenditure be unduly restricted. In the past years when money was scarce there had been a tendency to plan hospitals as small as might be; but, though the need for beds had not grown, Lord Nathan suggested that, with the coming of new techniques, the need for more space had grown greatly. He urged the Ministry when building new hospitals not to limit their building to the space actually needed at the moment but to exercise imagination and provide for the fresh disciplines and methods of tomorrow. We could not retain in this country the young men on whom the future of medicine depends unless we offered them the opportunity of developing their powers and their careers. Lord Nathan doubted whether the Ministry was justified in asking hospitals to contribute, for buildings, money from their endowment funds: private funds were being used to subsidise expenditure for which Parliament had made the Ministry responsible.

Lord AMULREE, speaking as a member of the medical staff of a London teaching hospital, agreed that during the past ten years the hospital service had improved. Many hospitals which had been rather poor were now very good, and there had been no corresponding falling-off in the work of the good hospitals. But he was a little frightened about the future. If too rigid a ceiling was placed on the amount of money available, then we were bound to get some kind of falling-off. Medicine was expensive work to carry out properly, and though one could economise one could not avoid spending money. At present there were many drawbacks in hospitals—for instance, operations had greatly increased in number and complexity, and many surgeons were now working under conditions of discomfort if not of difficulty. But, provided the staff and equipment were good, he did not think it necessary to have brand-new buildings to do good work; nor did he think that there was great need for more beds than at present. On the other hand, there was need for more accommodation for infirm elderly people who required care, though not in hospital.

Lord EVANS, in a maiden speech, said that his interest and occupation was with bedside medicine rather than administrative medical affairs. He was sure that the quality and standard of medicine must depend on the quality of the teaching hospital, and he pointed out that the teaching hospitals train most of the teachers of the ancillary services as well as undertaking their primary duties of the care of patients, the teaching of medical students, and research. Since the start of the N.H.S. little had been done for teaching hospitals save the provision of funds to keep the machinery going. They had outmoded inadequate accommodation for patients, teaching, and research. Of the twelve London teaching hospitals only two had ever been rebuilt, yet many had been badly blitzed during the war. Surely, he said, there must be some limit to the enjoyment of such austerities. Surely it was absurd for the teaching hospitals virtually to mark time till every other hospital caught up. The immediate past president of the Royal College of Surgeons of England [1] had suggested that hospitals should be encouraged to seek additional sources of finance outside the Government budgets of the N.H.S. For the teaching hospitals, to the minds of many, this would be a welcome return to old practices and in keeping with their heritage. In appealing to the community, to industry, and to philanthropic individuals they would follow the example of the universities, and such efforts might enable us in a few years to see several new teaching hospitals in this country.

Lord MORAN said that it was dangerous to measure the progress of a science by the foot-rule of the administrator, but he thought it just to congratulate the Ministry on a remarkable administrative achievement. They had decentralised the consultants in this country. Because consultants were paid for their hospital work it was no longer necessary for them to live in the great centres, and in almost every part of the country there were now specialists in every branch of medicine. Their number had also been greatly increased. Moreover the patient could not only see a consultant in hospital; if he was too ill to go there he could call a consultant to his house, and in 1956 there were 265,000 domiciliary consultations. Decentralisation had also made possible the upgrading of hospitals throughout the country. These two reforms would by themselves have justified the existence of the N.H.S., but the conditions in mental hospitals had also been transformed. Doors had been unlocked, the padded room was a thing of the past, 80% of the patients were voluntary boarders, and outpatient departments had been opened. People from America, the Commonwealth, and all over the world came to see how these institutions should be run, and it had been done without rebuilding.

REMUNERATION AND OPPORTUNITY

Another reform, Lord Moran continued, which the N.H.S. had brought was concerned with the remuneration of consultants. Before the service the consultant obtained his remuneration from private practice. Now most consultants got their remuneration for hospital work. A man about 40 would get £3255 per annum as a maximum basic salary, and for the rest of his working life he would get no more unless he was given a merit award. His material prosperity now depended on his professional efficiency, whereas formerly it was dependent to a great extent on his personality. There had, Lord Moran said, been many arguments for and against these awards, but of the bodies that had given evidence before the Royal Commission all save one had spoken in their favour. Turning to the future,

1. See *Lancet*, 1958, i, 1270; *Brit. med. J.* July 5, 1958, suppl. p. 5.

Lord Moran said that it was important not only that we should get the right quality of men into medicine; we should reward adequately those who submitted to the discipline and years of training to become a consultant. If the proper balance between the pay of the consultant and that of the general practitioner was not maintained, recruitment would wither. In the last resort the efficiency of the service would depend not on administration but on the quality of the entry and the training of the students. He admitted that he was uneasy about the quality of the entry. Not long ago middle-class parents paid for the fees of all medical students. Now two-thirds were maintained by the State and were selected by examination without any test or regard to character. He believed that one could not select people solely on examination for a profession like medicine which required the human touch more than almost any other.

He admitted that there was considerable discontent at present among general practitioners but he did not believe it was based on remuneration. The cause was to be found in the general decline of the status of general practice. It had begun when people who were seriously ill began to feel that they were well advised to go into hospital. It was mortifying to the doctors to find that the patient in a crisis preferred to put himself in the hands of a complete stranger. The N.H.S. had exacerbated this because, with consultants on their very doorstep, the general practitioners were unable any longer to make those modest excursions into the consultant field which had lent flavour to their life. In his view the remedy was for the pick of the general practitioners to follow their patients into hospital and to become part of the staff of the hospital. He believed that this should be the most important administrative move in the next decade. If that was not done, with a discontented profession, efficiency must wither, whatever the remuneration.

The Earl of CRANBROOK shared Lord Moran's hope that the general practitioner should be brought more and more into the hospital. But his own feeling was that the hospital needed to be brought more and more outside itself and into contact with the general practitioner and those who were serving the public in their homes.

ADMINISTRATORS, BOARDS, AND COMMITTEES

The Earl of LUCAN raised the question of hospital administrative staff. The Hall report had shown that the service was not offering a sufficiently attractive career to get the best type of administrator. Yet those who were responsible each year for several hundred million pounds of public money should be of the highest quality. On the training side there was a serious gap. A national scheme had been started a year or two ago, but the number of students was 24 and the course lasted three years. It could make only an infinitesimal contribution to the staffing problems of the 400 hospital boards. As a result, all the training these young men usually received was by being attached to different departments and different hospitals. It seemed to him that much more systematic and positive training was needed. Turning to the vexed question of capital investment and hospital building, Lord Lucan said that when he saw the millions of pounds being spent on office buildings, which were often put up for prestige purposes, he wondered if historians in a hundred years would not be puzzled how we could have got our priorities so wrong.

Viscount ASTOR asked for an inquiry into the administrative system of our hospitals. He felt that most hospital committees were far too big and that the work could be done by half the number of people in half the time. Members went into far too great detail on many minor matters which in ordinary administration should be done by a staff; and at the same time the ordinary house-committee had practically no responsibility for the hospital which it was supposed to know intimately. The hospital management committees were too big and proliferated so many subcommittees that it was difficult for any busy man to be a conscientious member. He believed that we needed small committees, meeting perhaps half as often, with chairmen and officials having greater responsibility for many minor decisions. We should try to recruit our hospital officials from a rather wider circle and be prepared to bring in some of those of great administrative ability who were being "axed" from the Services but yet had leadership and knowledge of organisation of people.

Another point was the almost complete separation of the medical and lay side. Some doctors sat on the management committee but no layman knew anything of what went on at the doctors' committees. So there were two parallel chains of committees both looking after the same hospital; "If one suggests that even the chairman of the hospital committee should go to the doctors' committee—well, my word!" He believed that there should be far greater confidence and mutual knowledge than at present.

THREE ACHIEVEMENTS

Lord STRATHCLYDE, replying for the Government, suggested that the magnitude of the undertaking was worth a little thought. There were in the hospital service in Great Britain some 3700 hospitals and clinics employing 374,000 full-time and 94,000 part-time staff, handling 4½ million inpatients and some 56 million outpatient attendances, and spending something like £400 million in a year. It was hardly to be expected that an undertaking of this size, financed from public funds, should not have thrown up many problems during the years in which it has been taking shape; but it would be grossly unfair to all the people running the service to give the impression that the Government were so preoccupied with the problems that required solution and the possibilities of the future that they had no time to spare for appreciation of what had already been done. Looking at the whole picture from the point of view of the central Government three features were notable.

First, the coming of the hospital service had resulted in specialised medical skill being much more widely available throughout the country. The number of specialists employed in the hospital services in Great Britain at the end of 1957 was not far short of 8000, an increase of nearly 33% on the figure even at the end of 1949 when the hospital service had already begun to make its impact. Mental health especially had gained by this. It was true that we still had not all the specialists we should like in this field, but an entirely new approach to the problems of mental illness has manifested itself in recent years.

The second feature was the sheer volume of the work that had been handled, compared with the very limited physical expansion that had been found possible. In these last eight years the number of inpatients had risen by 29% in England and Wales, and 43% in Scotland. There had been a 6% increase in the number of beds but this had been largely achieved, not by new building, but by bringing into use beds which were formerly idle. He did not want to give the impression that the Government did not consider that new building was necessary, but he thought it fair to give credit to the doctors, nurses, administrators and who, despite shortages and obsolescence, had yet achieved so much.

The third achievement was the progress made in the integration of the service. In 1948 nearly 3500 hospitals were taken over—many completely independent and separate, and others grouped only within a local-authority area. He had no doubt that there were still instances where it was far from perfect, but the service today was a reasonably coherent entity and not just a collection of individual hospitals.

Amendment of Registration Procedure

On July 2 Lord COHEN OF BIRKENHEAD introduced in the Lords the second reading of the Medical Act 1956 (Amendment) Bill which removes certain anomalies of the present system of medical registration.[1] He informed the House that the Bill had passed all its stages in the Commons without dissent, and that all interested parties had concurred in its provisions.

Royal Assent

The Opticians Bill and the Disabled Persons (Employment) Bill have received the Royal Assent.

1. See *Lancet*, 1958, i, 1340.

QUESTION TIME

Hospitals Staffing Working Party

Mr. KENNETH ROBINSON asked the Minister of Health whether it would be open to this Working Party to make recommendations on the levels of consultant staffing either in the country as a whole or in particular regions; and approximately how long he expected the Working Party would require to complete their task.—Mr. DEREK WALKER-SMITH replied: As the Working Party's task is to study the principles on which the medical staffing structure in the hospital service should be organised, they will not be concerned with the numbers of consultants as such. No estimate can be made yet of the time they will require, but I am sure they will proceed as quickly as they can. Mr. ROBINSON: Does the Minister not appreciate that the level of consultant staffing is a basic consideration, not only to the senior registrar problem but to everything else that the Working Party is supposed to be examining? Does he not realise that unless they can recommend on this matter these distinguished gentlemen will be wasting their time?—Mr. WALKER-SMITH: It is for these distinguished gentlemen themselves to decide what matters they will need to go into so that they can discharge the terms of reference, of which they are aware and which they have accepted.

Mr. ROBINSON asked the Minister why he did not include either a psychiatrist or a layman with special knowledge of the staffing structure requirements of the mental hospitals among his nominees on the Working Party.—Mr. WALKER-SMITH: The reason is that the Working Party as constituted is well equipped to cover the hospital service generally and is free to obtain evidence about particular classes of hospital, mental and others. Mr. ROBINSON: Is the Minister not aware of the indignation which is felt among psychiatrists at the way they have been excluded from this important body? Does he not realise that the needs of the mental hospitals, even concerning the staffing structure, may be very different from those of general hospitals? Will he not reconsider the matter?—Mr. WALKER-SMITH: I am not aware of any such indignation. To give representation to all the various specialties and to the different kinds of hospitals which would logically follow, would only increase the size of the Working Party far above the number of 12 and would certainly have delayed the results of its proceedings. Dr. EDITH SUMMERSKILL: This is a curious omission, because the hospitals which are grossly overcrowded in every area are the mental hospitals. The main problem very often is lack of staff or the proper allocation of staff. Therefore, to omit a psychiatrist from a committee which is considering the overall allocation of staff is a little peculiar.—Mr. WALKER-SMITH: The Working Party consists of people all of whom have great experience in the hospital service. They can, I am sure, be trusted to obtain such information as they will need in regard to all the particular classes of hospitals and specialties with which they are concerned. Mr. ROBINSON: In view of the unsatisfactory nature of this and the previous reply, I give notice that I will raise the matter on the adjournment.

Inspection of Imported Egg Products

Mr. ARTHUR BLENKINSOP asked the Minister what action he was taking to ensure that imports of egg white were fully inspected before release to manufacturers.—Mr. RICHARD THOMPSON, parliamentary secretary to the Ministry, replied: Port health and other local authorities have been asked to pay special attention to the sampling of imported egg products for bacteriological examination. At present the authorities try, whenever possible, to sample every batch. It would not, of course, be practicable to sample every tin. Mr. BLENKINSOP: Does the Minister not agree that the reports from his own Ministry show there is a large proportion of samples taken which show a high level of infection?—Mr. THOMPSON: Yes, we recognise that there is a problem here, but we consider that the present arrangements for sampling are the best we have tried and also that the wish which we have made known to the exporting countries ought to provide a solution.

In England Now

A Running Commentary by Peripatetic Correspondents

IN our early youth we were sick on the second storey of the Eiffel Tower, and since this incident we have had little taste for heights. It is difficult to persuade us to enter an aircraft or even to paint the dining-room ceiling, and on our seaside holidays we are a skeleton at the feast. While our dependants skip gaily along the smugglers' path, dislodging loose stones into the gulf 300 feet below, we are to be found progressing carefully on hands and knees, gripping the landward vegetation in an ecstasy of spasticity.

We were therefore disturbed to find during our last summer holiday that family opinion had committed us to visiting a lighthouse. Our confidence in the outcome was not enhanced, after we had battered our way in a 50-knot wind to the foot of the structure, by the discovery that we were expected to sign away our chances of survival in advance. "I the undersigned", said the form sombrely, "hereby acknowledge agree and undertake for myself and for and on behalf of all minors noted hereunder as under my sole charge that no action suit claim or demand shall lie or be made or instituted in respect of any accident death injury loss or damage sustained or occurring by or to us or to any of us during the said visit. I will indemnify", went on the form, clinching the matter, "keep indemnified and save harmless all departmental servants officers and agents against all actions suits claims and demands . . ."

The lighthouse-keeper was sleeping, and his assistant was seeing a man about a wreck, but trustingly permitted us to make the ascent unaccompanied. The minors under our sole charge occupied themselves happily in counting the 329 steps, and no accident death injury loss or damage was sustained or occurred on the way up. In the lantern room, however, the rarefied air and the presence of several other minors had the worst possible effect. Within seconds the lens holder, bearing the legend ON NO ACCOUNT TOUCH THE LENS HOLDER, had been seized and was rotating madly on its axis to the accompaniment of wild cries of exaltation. A dissipated-looking minor of a reflective turn of mind had begun to try to drop marbles on the head of the assistant keeper, and a small ginger group was running at high speed round the outside gallery, restrained from falling into the immeasurable depths only by a single rail at chest height. After one vertiginous glance through the open door we were forced to concentrate on the lighthouse keeper's box of dyspepsia tablets under the map of the local rocks and reefs. While we were thus engaged, the door to the outside gallery slammed and locked itself; the minors under our solé charge, happening to be on the wrong side at the crucial moment, set up a prolonged bawling. With set and pallid face we descended the steps to fetch the assistant keeper with a key.

When order had been restored and we had indemnified and saved harmless the assistant keeper, we reached the ground again in an atmosphere of mutual congratulation. Only too soon a rough count established the fact that our personal quota of minors had been reduced by one. Elected a search party by popular acclaim, we climbed the 329 steps for the third time, to find our youngest minor flat on her stomach in the lantern room, deeply immersed in the lighthouse keeper's *True Love Stories* and sampling his dyspepsia tablets.

For our next holiday we are going to the Cotswolds.

* * *

I suppose this week most of us have been looking back over the past decade and asking ourselves how we have fared. According to the popular press we G.P.s have had a raw deal. We are the underdogs of the health service and our yelps for fair play against those bloated plutocrats the consultants should wring the heart of every honest man. We work twenty-four hours a day. We even have to pay to get a holiday. We are bullied by our patients and are treated with contempt by the hospitals.

Why then, despite all these horrors, are there dozens of applications for every vacancy in this underdog service?

Is it possible that the Press is not quite accurate in its accounts of our miseries? Perhaps some of us do see eye to eye with our friends the consultants. Perhaps, though of course we wouldn't mention it, most of us love our work. Perhaps we enjoy treating our fellow men in their own homes, even though it means long hours and short holidays. Perhaps, though we hardly dare whisper it, some of us feel that general practice has gone forward during the last ten years and we are proud of it.

* * *

Everyone knows how enlightened and progressive mental hospitals are these days; but I was still unprepared for the reaction of a colleague who was trying to interview patients, in what would once have been called a "back ward", despite frequent interruptions from a character who in a less permissive era would almost certainly have been stowed safely away in a padded cell. Losing patience at last, he flung down his pen and exclaimed indignantly, "Really, Sister, this place is getting to be like a madhouse."

* * *

It is obvious to those who read the literature that getting satellites into space is a matter of stages. We didn't actually get anything into orbit. Initial trials were carried out with 6*d*. and 3*d*. rockets. The smaller rocket was fixed to the larger so as to allow only an upward separation. Firing of the second stage was by a predetermined length of catherine wheel, which was inserted into the vitals of the smaller rocket. When the bugs had been ironed out of this phase the final trial was carried out with a 2*s*. 6*d*., a 1*s*., and a 3*d*. rocket. This is only one stage short of space according to junior's calculations. We were reduced to one test vehicle because of lack of enthusiasm in the female part of the family, who did not like catherine wheels being cut up and refused to allow more than one 2*s*. 6*d*. rocket.

This was fired on Guy Fawkes night last year. The countdown went according to plan. The first stage was fired as the fuses of the other two were lit. Unfortunately the smallest rocket fell off, its connections being apparently strong enough only for 6*d*. boost, but the other two stages were away. The end of the first boost was marked as planned by a display of green stars. There was a delay of the cut-in of the next motor, probably because we had to use a different make of catherine wheel to our usual. The second stage could be just seen as a faint gold spot curving over and gradually increasing speed as it fell. Nearing the ground it burst into life and gathering momentum at an alarming rate hit a distant neighbour's roof and disappeared. There was a far-off crash of falling tiles, then silence. The third stage burst into life and vanished into the potting shed. We crept indoors. We are now talking to our neighbour again. It had gold stars, apparently.

* * *

BEFORE AND AFTERTHOUGHTS

I thought I saw an A-line
A-twisted all awry.
I looked again and saw it not
—I cannot tell you why.

I thought I saw a Newton
In thought upon the shore;
I looked again and saw it was
A man I could ignore.

It seemed I saw a System
Of thoughts all bright and new;
I looked again and saw they were
A muddled, motley crew.

I thought I saw Time's chariot,
Wing'd horses all before;
But after, when I looked again
They were in front no more.

Had we but world enough and space
These theories, Doctor, were in place;
Do write again, but ere you start
Put Reason's horse in front of Fancy's cart.

Letters to the Editor

ORTHOPÆDICS, INDIVIDUALITY, AND THE HOSPITAL SERVICE

SIR,—At a time when we are reviewing the work of the past ten years I should like to stress the tradition of individual effort and the difficulty of giving it expression in the hospital service today. The difficulties are largely inescapable when control is in the hands of coordinating committees and administrators largely out of personal touch with the day-to-day work of hospitals, and for whom organisation, centralisation, integration, and rationalisation are prominent thoughts. Tradition should not slavishly be followed: many traditions hold bad features. The Ministry of Health has, however, been right in emphasising the need to preserve the good traditions of the voluntary hospitals (though it is often very difficult for the house committees of these hospitals themselves to maintain them). The idea often is given no more than lip service.

I am worried by the discouragement of a sense of responsibility and initiative at the periphery and particularly worried by a tendency to destroy certain valuable schemes of hospital service which, in advance of their day, were built up by the enlightened and creative efforts of pioneers like Robert Jones and Henry Gauvain. Naturally I take the orthopædic service, for it is the one I know best and because (as I pointed out in *The Lancet* in 1944 [1]) it possessed features which we can now see foreshadowed many of the developments of the national hospital service itself.

It is unfortunate that orthopædics is often thought of as a purely surgical special branch of medicine. If it were so there would be some excuse for regarding the orthopædic idea of segregation, teamwork, continuity of treatment, and rehabilitation as an anachronism in special hospital units. On the contrary, orthopædics is a very general rather than highly specialised branch containing a dominant interest in medicine itself. Sir Henry Gauvain, who started his work at Alton fifty years ago, exemplified one aspect of this physician's outlook and he built up a splendid institution. At Oswestry, Oxford, Stanmore, and Pyrford similar organisations were established by the pioneers. They involved a compact organisation of a central hospital fed from and feeding into dispersed outpatient clinics with a team of surgeons and their specially trained groups of aftercare sisters, orthopædic nurses, secretarial staff, workshops, &c. In each the emphasis varied and the model was that at Oswestry. These schemes and others like them (and indeed others which still *should* be established) have a special approach to the whole man (starting with childhood), his social background, and the continuity of his treatment leading to rehabilitation.

The compactness of the organisation with its individual leadership and fine teamwork is now faced with a changing clinical responsibility. Although tuberculosis, rickets, osteomyelitis, and, we expect, poliomyelitis are diminishing, nevertheless the congenital and developmental anomalies of childhood, trauma, arthritis, and the locomotor lesions of stress will continue to provide a large number of long-term problems for which treatment in these schemes is well found. It would not be right to say that there is great overt evidence of destruction, yet in this-and-that small way, orthopædic institutions are being eroded. There is loss of individual identity, and the consequent weakening of morale, lack of proper support for the training and wellbeing of the orthopædic nurse and aftercare sister, and the separation of sections of the work of an organisation into the hands of new consultants working largely in isolation from the parent team, which results in dispersal of clinical material.

1. Capener, N. *Lancet*, 1944, ii, 355.

This dispersal may be considered to be countered by the association of the orthopædic surgeon with his general medical and surgical colleagues in local units and by the association of the patient's treatment nearer his home. Of course orthopædic surgeons should be part of the team in every general hospital, but this need not be incompatible with his belonging to another team as well. A patient's separation from the neighbourhood of his home has disadvantages but is less of a problem now than it was thirty years ago, and in any case is outweighed by the advantages of the greater experience and skill to be achieved in the special hospitals, particularly when these have an efficiently coordinated aftercare clinic system.

I am not so senile as to think that these orthopædic-hospital schemes could not be improved. What I do say is that it is very difficult to do the necessary individual creative work in the atmosphere of central group administration.

There is one final point. The orthopædic services of this country are the envy of foreign visitors, who so often have nothing of the sort. We owe it to the new Commonwealth nations to maintain and develop this type of organisation. Abroad they still see tuberculosis and other crippling diseases in the dreadful form that we did thirty and more years ago, and their young men come to us to learn.

Exeter. NORMAN CAPENER.

N.H.S. STAFF COLLEGE

SIR,—The suggestion from Dr. Parker (July 5) of a National Health Service Staff College is to be warmly welcomed. We should, however, hesitate before advocating a Staff College exclusively for members of the profession. We need to see an end to the rivalries for administrative authority. At the last annual conference of the Institute of Hospital Administrators, it was sad to hear how much time was given to discussion of who was responsible to whom. This, no doubt, is a natural preoccupation among lay administrators still looking over their shoulders to the days when medical superintendents were all-powerful figures in every aspect of hospital responsibility, but it is an attitude which stultifies initiative and innovation.

The most advanced sectors of industry today have long recognised the vital contribution which technical training and background can make to administration. The second industrial revolution we are witnessing today is being directed by a partnership of "lay" and technically trained management, applying the new knowledge of technology, operational research, and social science with an effective enthusiasm from which the Health Service has much to learn.

After ten years of reaction against medical administration in the service, a new balance needs to be reached and a working partnership created between medical, nursing, and lay personnel. An exclusively medical staff college may accentuate rather than resolve the existing divisions.

The Administrative Staff College of the King Edward Hospital Fund is carrying out an imaginative and stimulating task, almost entirely among the lay staff of management committees. The fund also runs a college for administrative nursing staff. Could not the present Staff College be expanded to cater jointly for medical and other administrators? I believe that a Joint Staff College, in addition to its function of training in the techniques of modern management applicable to a health service, would do much to define each partner's proper sphere of activity, and to infuse that sense of common purpose which the service so badly needs.

Paddington General Hospital, London, W.9. J. FIELDING Medical Director.

DEATH OF A BOXER

SIR,—I have followed the correspondence upon the medical complications of boxing with mixed feelings. Dr. Lyburn's last letter (July 5) goads me into reply, however.

Surely among his boxing friends and acquaintances he has encountered traumatic progressive encephalopathy. There now exists really quite a formidable literature upon the subjects of punch-drunkenness; on death in or shortly after a boxing bout; as well as on the occurrence of subdural hæmatomata and of traumatic carotid occlusion as a result of boxing. The ophthalmic literature alone contains an impressive record of injuries to the eye.

London, W.1. MACDONALD CRITCHLEY.

REVERSAL OF SUXAMETHONIUM PARALYSIS WITH NEOSTIGMINE

SIR,—Dr. Shegog Ruddell reports an instance of neostigmine-reversible suxamethonium paralysis in a child, and demonstrates once more that anticholinesterase decurarising drugs may be used with confidence in these circumstances.[1]

In 1954 I drew attention to the fact that young children were inherently resistant to suxamethonium,[2] and in 1955 confirmed this, showing that the characteristic was unrelated to cholinesterase activity, and probably associated with no physical factor other than an inherent "state".[3] I am sure that had the biochemical estimations, including the serum-cholinesterase, been forthcoming in Dr. Ruddell's patient, they would have been essentially normal. More recently, with others, I suggested that changes in sensitivity to depolarising relaxants were more likely to occur in those patients showing an inherent resistance to the drug in the first instance.[4] The clinical sequel of these two observations (that the young are prone to develop a "dual" response after depolarising agents) has been noted by Rees.[5]

Better terminology would clarify the situation in the minds of many of us. The terms "depolarising" relaxants, and "dual" response are misleading. The expression biphasic response, illustrating consecutive rather than concurrent actions, would seem preferable.[6] The second phase of this response represents the typical, and to be expected, non-depolarising effects of the so-called "depolarising" agent, and may be recognised and treated as such with confidence.

In the presence of a raised endplate resistance to depolarisation the typical action of suxamethonium, already previously described,[7,8] is slower in onset, less intense in effect, but mildly prolonged. In this phase, if attempts are made to obtain (with the less effective agent) the immediate and profound relaxation usually associated with the depolarising action of suxamethonium, accumulative effects and further delay in recovery may follow. This depression is reversed by anticholinesterase drugs.

These circumstances do not contraindicate the use of suxamethonium, providing it is recognised that a slightly longer-acting and less effective "non-depolarising" agent is being administered, and precautions are taken to avoid overdose. Antidotes should be used whenever indicated.

1. *Lancet*, 1958, i, 1390.
2. Hodges, R. J. H., Harkness, J. *Brit. med. J.* 1954, ii, 18.
3. Hodges, R. J. H. Proceedings of the World Congress of Anæsthesia *Curr. Res. Anæsth.* 1956, p. 247.
4. Foldes, F. F., Wnuck, A. L., Hodges, R. J. H., Thesleff, S., de Beer, E. J. *ibid.* 1957, **36**, 23.
5. Rees, G. J. *Brit. med. Bull.* 1958, **14**, 38.
6. Hodges, R. J. H., Foldes, F. F. *Brit. med. J.* 1957, i, 373.
7. Hodges, R. J. H. *ibid.* 1956, ii, 1240.
8. Hodges, R. J. H. *ibid.* 1958, i, 1416.

A non-depolarising block following the administration of suxamethonium may be anticipated not only in children and neonates. It may be expected to arise whenever endplate resistance to depolarisation is present, inherently as in certain species, pathologically acquired as in myasthenia gravis and sometimes electrolytic imbalance, or induced (particularly in those with an inherent tendency) by drugs. This last may follow the administration of relaxants,[4] but may also follow the administration of drugs with no obvious clinical neuromuscular-blocking effects (e.g., oxytocin).[5]

Portsmouth. R. J. HAMER HODGES.

ANÆSTHESIA FOR THE EMPHYSEMATOUS

SIR,—In an annotation [1] you summarise the hazards of general anæsthesia and artificial ventilation in emphysematous patients. The article goes on to say that despite its drawbacks artificial ventilation " is generally advisable for emphysematous patients undergoing extrathoracic operations as well [as thoracic operations,] since it is the only means of ensuring adequate gas exchange ".

It is unfortunate that your article dealt exclusively with general anæsthesia, and that regional anæsthesia, either alone or in combination with light general anæsthesia, should not have been mentioned, for the latter provides good operating conditions, as well as adequate respiratory exchange in most cases. Admittedly, in thoracic and upper-abdominal operations under regional anæsthesia, suppression of intercostal activity demands the use of controlled respiration just as in non-emphysematous patients, but in operations elsewhere adequate spontaneous respiration can usually be retained; if in doubt ventilation can be measured directly by switching a simple spirometer into the anæsthetic circuit from time to time.

The retention of adequate spontaneous respiration has definite advantages, for while it exists the normal inflationary pattern of the chest is maintained, and alveolar ventilation-perfusion ratios remain relatively unaltered. But, as Campbell et al.[2] point out, the imposition of artificial respiration is accompanied by an increase of physiological dead-space, and the hazards outlined in your article are added to this. Besides the difficulties you mentioned there is some evidence that under light general anæsthesia and neuromuscular blockade surgical stimulation reduces the compliance of the lungs, so that the work of breathing is increased, and higher intrathoracic pressures have to be used to shift a given volume of gas.[3]

The neuromuscular-blocking agents have made general anæsthesia so simple and safe that the pendulum has swung away from the more exacting methods of regional anæsthesia, which are falling into disuse. Consequently, the present generation of anæsthetists-in-training find it difficult to obtain a good practical grounding in regional techniques, although these still have much to offer, especially in the emphysematous patient. Unfortunately skill in regional methods requires practice, and this is not always easy to obtain when slickness of " throughput " is so often the primary aim in many operating-theatres. But consultant anæsthetists should see to it that their juniors do get the opportunities to achieve facility with regional techniques; otherwise the disciplines of the specialty will become depressingly narrowed.

Royal Victoria Hospital, Montreal. P. R. BROMAGE.

SIR,—The remarks in your annotation of June 14 are very timely. Extensive experience has shown that artificial respiration is imperative for all such patients undergoing major operations under general anæsthesia—regardless of the site of operation.

A few points may be re-emphasised: the administration of bronchodilator drugs should be an integral part in the maintenance of anæsthesia; and the rate of respiration and tidal volume should be monitored, together with the airway pressures. These parameters may be accurately determined before induction of anæsthesia on the basis of the size and age of the patient, together with an estimate of degree of emphysema (simply determined by the breath-holding test and expiration time).[1] These must be adjusted according to the posture assumed by the patient to facilitate the work of the surgeon.[1]

When these measures are employed, emphysema presents no problems in oxygenation or carbon-dioxide elimination, and spontaneous respiration is resumed quickly at the end of the anæsthetic if care has been taken to establish a light level of analgesia, hypnosis, and muscle relaxation.

Department of Anæsthesia, University Hospital, Saskatoon, Saskatchewan. ALLEN B. DOBKIN.

LIPOPROTEIN PATTERNS IN MYOCARDIAL INFARCTION

SIR,—In reviewing the excellent article by Dr. Elspeth B. Smith [2] I was much impressed by the correlation between the characteristic lipoprotein band, the pre-β-lipid found associated with myocardial infarction, and the S_f20–100 part of the standard S_f12–400 class of lipoproteins of Gofman.

In our attempts to reverse existing atherosclerosis and to lower the levels of both S_f0–12 and S_f12–400 lipoproteins, as well as cholesterol levels, it has been virtually impossible to lower the S_f20–100 and the S_f100–400 parts of the standard S_f12–400 class of lipoproteins without carefully screening out all products of hydrogenation.

Niacin (nicotinic acid), fresh thyroid extract, low-natural-saturated fats and low-cholesterol intake, plus 2–3 ounces daily of corn oil (mazola) or 12 capsules daily of 750 mg. safflower oil by mouth, have been given to supply additional unsaturated linoleic acid. All products of hydrogenation were excluded, and replaced in all baked or fried foods by the essential unsaturated linoleic acid in the form of corn oil. By this means it has been possible to reduce rapidly cholesterol and both groups of lipoproteins.

Nicotinic acid was given in total daily dose of 3 g. divided and after meals, and the fresh thyroid extract was started at usually no less than gr. 3 and raised to gr. 6 or more depending upon the lipid-lowering response.

All our lipoprotein patterns were air-mailed the same day to the Gofman group at the Institute of Medical Physics at Belmont, California, for ultracentrifuge analysis, and all patterns are there recorded by number. Dr. Holly Heitzman, clinical director of St. Mary's Hospital, Green Bay, secured the blood samples for a portion of this study, and Dr. John Ford, clinical director of St. Vincent's Hospital, Green Bay, secured the remaining group of blood samples. Both hospital groups are now correlating the total cholesterols, atherogenic indexes, and diastolic and systolic pressures.

The following is a typical case, in which the intelligent cooperation of the patient was secured in this simple approach to the possible reversal of atherosclerosis:

A 53-year-old woman weighing 163 lb. had a blood sample taken on March 12, 1958: fasting cholesterol 200 mg. per 100 ml.; S_f0–12 413 mg. per 100 ml., S_f12–400 844 mg. per 100 ml.; atherogenic index 189; blood-pressure 190/110 mm. Hg.

On May 1 the findings were: weight 146 lb.; fasting cholesterol 140 mg. per 100 ml.; S_f0–12 245 mg. per 100 ml., S_f12–400 62 mg. per 100 ml.; atherogenic index 35; blood-pressure 104/76 mm. Hg.

1. *Lancet*, 1958, i, 1261.
2. Campbell, E. J. M., Nunn, J. F., Peckett, B. W. *Brit. J. Anæsth.* 1958 **30**, 166.
3. Bromage, P. R. *Clin. Sci.* 1958, **17** 217.

1. Dobkin, A. B. *Brit. J. Anæsth.* 1958, **30**, 282.
2. *Lancet*, 1957, ii, 910.

Of the utmost clinical significance during this study, which has been correlated with the Gofman group since November, 1957, has been the inability to produce any considerable lowering of the S_f12–400 class of lipoproteins without carefully screening out all products of hydrogenation.

At this point it definitely seems that the unnatural unsaturated fatty acids with a high melting-point, which are the products of hydrogenation, may be a most important factor and in all probability are not reflected in the total cholesterol estimation, and fall into S_f20–100 and the S_f100–400 parts of the standard S_f12–400 class of lipoproteins.[3] There is little doubt that a large part of human disease is due to physiological chemical imbalance, but it is apparent that the body cells can recover to an amazing degree from these chemical upsets.

Green Bay, Wisconsin. WARREN T. HAGERTY.

THE ÆTIOLOGY OF LEUKÆMIA

SIR,—Your leading article of July 5 might be criticised on the grounds of incompleteness; but it would not be possible to meet this criticism in less than a large tome. It could be argued that the title was misleading and should have been the Virus Theory of Murine Tumours; and it is certainly odd to find no reference to, among American workers, Kaplan and Law and only one, purporting to support Gross, to Furth. However, accepting the thesis that Gross and Stewart and Friend have produced extremely powerful evidence in favour of viral agents being intimately involved in the development of various murine neoplastic diseases, or, as they might argue, causative, it must seem ludicrous to them to read your conclusions, (*a*) that an impasse has been reached, whereas in fact the field is developing so fast that even you, Sir, seem not to be abreast of recent multitudinous advances, and (*b*) that, an infective agent having now, you infer, been isolated and categorised, there is little that can be done about it. Oh, Koch!

Atomic Energy Research Establishment, Harwell, Berks. J. F. LOUTIT.

EXPERIMENTAL PRODUCTION OF ENDOMYOCARDIAL FIBROSIS

SIR,—I write to correct a statement attributed to me, by Professor Selye in his interesting paper.[4]

I was quoted as saying that 40% of patients with heart-disease, admitted to hospital in Eastern Nigeria, have endomyocardial fibrosis. This statement was apparently based on my personal communication to Dr. Brigden, to which reference was made in his St. Cyres lecture.[5]

What Brigden said was: "Nwokolo has seen the condition (of endomyocardial fibrosis) in Eastern Nigeria, where he finds that 40% of cases of heart-disease admitted to hospital are cardiomyopathies." In that lecture, Brigden used the term cardiomyopathy to include obscure cardiopathies such as congenital cardiomyopathy, nutritional heart-disease, alcoholic heart-disease, amyloidosis, collagen diseases of the heart, infective myocarditis of all kinds, endomyocardial fibrosis, and other cardiopathies of unknown ætiology. It is clear therefore that Brigden did not use the term cardiomyopathy to mean endomyocardial fibrosis only, as Professor Selye's usage seems to imply.

In my communication to Dr. Brigden, I referred in part to a publication[6] in which I reported cases of endomyocardial fibrosis confirmed at necropsy, as well as other cases in patients who died of congestive cardiac failure but in whom no fibrosis was found at necropsy. The figure of about 40% referred to the proportion of cases of obscure cardiopathies in relation to the total number of cardiac admissions into the General Hospital, Enugu, Eastern Nigeria, in a small series of cases.

My view is that endomyocardial fibrosis constitutes a mere fraction—probably under a third—of these obscure cardiopathies.

London, S.W.18. C. NWOKOLO.

3. Griffith, W. H. *J. Amer. med. Ass.* 1957, **164**, 411.
4. Selye, H. *Lancet*, 1958, i, 1351.
5. Brigden, W. *ibid.* 1957, ii, 1243.
6. Nwokolo, C. *W. Afr. med. J.* September, 1955, 103.

CORTISONE IN THE TREATMENT OF ACUTE MILIARY TUBERCULOSIS

SIR,—I was pleased to read that Dr. Lambros[1] has successfully treated a case of miliary tuberculosis using cortisone with the antituberculous drugs.

A case of miliary tuberculosis and meningitis in a patient who was also hypersensitive to streptomycin was included in a series of cases of active tuberculosis treated by corticotrophin and chemotherapy which I published in 1954.[2] This patient remains completely well six years later.

Harefield Hospital, Middlesex. L. E. HOUGHTON.

ANKYLOSING SPONDYLITIS AND CHRONIC INTESTINAL INFLAMMATION

SIR,—Forestier[3] and Romanus[4] mentioned an association between ankylosing spondylitis and inflammatory intestinal disease, and Steinberg and Storey[5] have reported 6 cases. I have seen 3 examples of this association.

CASE 1.—A man, aged 31, was admitted to Frenchay Hospital in 1957. He had pain in the lumbar region and left leg, which had started some seven months previously and had been treated, by physiotherapy and a plaster-of-paris jacket, with improvement. He also had diarrhœa, which had started suddenly seven weeks previously, with bowel action 18–20 times daily, very loose, and frequently containing blood and slime. He had had previous episodes of diarrhœa in 1943 and 1944.

The left side of his abdomen was very tender; movements of the lower thoracic and lumbar spine were limited and straight leg raising was restricted on the left. Hæmoglobin was 54%, erythrocyte-sedimentation rate (E.S.R.) 60 mm. in the first hour (Wintrobe). Sigmoidoscopy showed a reddened mucosa but no ulceration in the rectum. A radiograph of the spine showed partial obliteration of the sacroiliac joints and some calcification in the anterior spinal ligament; this was regarded as typical of ankylosing spondylitis. A barium-enema examination showed very extensive changes involving almost all the large bowel; and these were typical of ulcerative colitis.

The patient improved on treatment with corticotrophin and was later given a course of radiotherapy to the spine after transfusion had corrected the anæmia.

Diagnosis.—Ankylosing spondylitis and ulcerative colitis.

CASE 2.—A man, aged 59, was admitted to Frenchay Hospital in 1954 complaining of loss of weight and pain in the back and neck of two years' duration. He was pale and wasted, and had considerable limitation of all spinal movements. Hæmoglobin was 70%, E.S.R. 60 mm. in the first hour, colour-index 1·3. The marrow showed a few megaloblasts but mainly a normoblastic picture. Stool examination showed definite steatorrhœa. Radiographs of the spine showed fusion of both sacroiliac joints and calcification of the spinal ligaments. Barium-enema examination showed no definite abnormality.

He made good response to treatment with folic acid, iron, and calciferol, and his hæmoglobin rose to 94%. He was later

1. Lambros, T. A. *Lancet*, 1958, i, 1370.
2. *ibid.* 1954, i, 595.
3. Forestier, J. *Radiology*, 1939, **33**, 389.
4. Romanus, R. *Acta med. scand.* 1953, **145**, suppl. 280.
5. Steinberg, V. L., Storey, G. *Brit. med. J.* 1957, ii, 1157.

given a course of radiotherapy which eased his spinal pain considerably.

Diagnosis.—Ankylosing spondylitis and steatorrhœa of unknown cause.

CASE 3.—A man, aged 53, was admitted in 1957 to Southmead Hospital for investigation of bouts of diarrhœa which had begun three years previously. The motions were at times very offensive and contained blood and mucus. He had been under treatment for ankylosing spondylitis since 1946.

Spinal movements were much limited and occult blood was present in the fæces. Hæmoglobin was 84%, E.S.R. 46 mm. in the first hour. Radiographs of the spine showed bridging between the bodies of the lumbar vertebræ. Barium-meal and follow-through examination showed a definite irregularity of the terminal ileum, of the type seen in regional ileitis.

His diarrhœa settled when codeine was given orally, and his general condition improved in hospital.

Diagnosis.—Ankylosing spondylitis and Crohn's disease.

In these 3 cases, chronic intestinal disease was associated with ankylosing spondylitis, and it is my impression that this association is not one of chance.

I should like to thank Dr. J. M. Naish for permission to publish these cases.

Department of Medicine,
Frenchay Hospital, Bristol. S. G. FLAVELL MATTS.

THE TOURNIQUET

SIR,—In your leading article of May 31 and in Professor Pannett's letters of March 15 and June 14, certain categorical condemnations of the tourniquet are made. While it is true that there is an increasing tendency for limb surgery to be undertaken without the tourniquet, the time has not yet come when it could or should be completely discarded.

Professor Pannett's experiences of "enormous œdema when the tourniquet is removed" and his view that "infection is likely to establish itself more easily" are not paralleled by the experience and opinions of many orthopædic surgeons. It is possible, for example, to use below-knee tourniquets for foot operations with full hæmostasis but without getting peroneal palsies if the "Esmarch's" bandage is accurately applied. Infection of clean wounds is rare in orthopædics and is no commoner in, for instance, knee operations done with a tourniquet than in hip operations done without. Again, post-operative œdema need not follow, particularly if the surgeon himself puts on the bandages, not leaving it to the most junior person in the theatre.

While I entirely agree with your reiterated warnings on the use of the tourniquet, I cannot agree with ex-cathedra pronouncements (such as "There is no place for below-knee tourniquets") which can only cause embarrassment to some and give universal condemnation to a procedure which continues to have a place in the right hands.

Mr. I. S. Smillie once said, in reply to a charge that one of his instruments was dangerous: "All surgical instruments are dangerous unless they are used properly." The same applies to the tourniquet.

Canterbury. F. G. ST.CLAIR STRANGE.

RECORD OF EXPOSURE TO RADIATION

SIR,—At the present rate of nuclear-weapon tests we shall soon have reached the point of no return as far as the limit of safety to radiation exposure is concerned. This is a grim state of affairs about which the medical profession can do little more than indicate the risks and dangers.

We have, however, a grave responsibility in deciding whether our patients should be exposed to further radiation in the form of diagnostic X rays. I have for long been concerned at the casual way in which these investigations are carried out, usually with no regard to the number and cost of films taken in the past and often with insufficient consideration to the question "is this procedure really necessary?"

It seems to me that the time has now arrived when every patient should have some sort of simple record card whereon is shown the total amount, as far as it can be estimated, of previous radiation to which he has been exposed and where can be recorded subsequent amounts at the time the films are taken.

Royal Salop Infirmary,
Shrewsbury. A. W. J. HOUGHTON.

INFLUENCE OF LIGHT ON THE HYPERBILIRUBINÆMIA OF INFANTS

SIR,—I was very interested in the paper on the above subject by Dr. Cremer and his colleagues,[1] and their effort to use light for the reduction of hyperbilirubinæmia. Their observation that serum-bilirubin is photosensitive was also noted by me and recorded, in a paper on the Technique and Interpretation of the van den Bergh Test, in the *Irish Journal of Medical Science* for September–October, 1927, when I said: "Sera to be examined should not be exposed to bright sunshine."

Dublin. R. E. STEEN.

CERVICAL AORTIC ARCH

SIR,—It would seem desirable to make a plea against the term "cervical aortic knuckle" to describe the aortic-arch anomaly noted by Professor Lewis and his colleagues.[2]

It is the summit of the arch itself which is seen pulsating in the neck, whilst "knuckle" might imply an aneurysmal dilatation of the arch which projects. The term is undesirable also in that it carries an ætiological suggestion of the aortic arch having spilled or "knuckled" out of the chest. Embryological considerations refute this possibility and show that the arch is, in these cases, a cervical structure.

In January, 1957, a 35-year-old certified mental-defective man, having a right upper mediastinal shadow on a mass radiograph, associated with a pulsatile swelling on the right side of the neck extending to the hyoid cartilage, was admitted to hospital. Compression of the mass produced obliteration of pulses in the right arm and both femoral arteries, whilst those in the left arm remained. Manometric tracing of this diagnostic obliteration of femoral pulse was obtained; and the anatomical features of the convoluted, right-sided aortic arch in the neck were demonstrated by retrograde aortography. These appearances differed from the post-mortem findings of Beavan and Fatti [3] in that the left subclavian artery arose from a left innominate artery, the first branch of the arch, whilst in their case the left subclavian was the last major branch of the arch. No evidence of dyspnœa nor dysphagia could be obtained and the patient remains under observation. This case was presented with cine-photography of the swelling by Mr. R. Abbey Smith at the summer meeting of the Thoracic Society in 1957 and a detailed report and analysis are being prepared.

It should be remarked that in all three patients noted to have this condition, the cervical aortic arch has been right-sided, and the descending aorta left-sided. Reid [4] described an anatomical dissection in which a right aortic arch "ascends through the superior aperture of the thorax into the root of the neck and must have given rise to marked supersternal pulsation".

1. Cremer, R. J., Perryman, P. W., Richards, D. H. *Lancet*, 1958, i, 1094.
2. Lewis, C., Harley, H. R. S., Rogers, L. C. *Lancet*, 1958, i, 1340.
3. Beavan, T. E. D., Fatti, L. *Brit. J. Surg.* 1947, **34**, 414.
4. Reid, D. G. *J. Anat., Lond.* 1914, **48**, 174.

Notably, also, the cases of abnormally high thoracic aortic arch recorded by Tori [5] and Mr. Norman Barrett's case [6] have been right-sided. The embryological grounds for this right-sided nature are perhaps less readily acceptable than the reasons for a cervical arch; and it is noteworthy that, in the offspring of vitamin-A-deficient rats, Wilson and Warkany [7] found the condition twice on the left, three times in a double aortic arch, but never singly on the right, though in all cases there were also other variations of the arch pattern. Nevertheless, and at least until a left-sided case is recorded, it seems reasonable to describe the condition now recognised as " right-sided cervical aortic arch ".

Dysphagia developing for the first time in middle age owing to ring-like formation raises particular consideration in these cases. Both dysphagia and dyspnœa may present during infancy from vascular rings. Dysphagia, without dyspnœa, developing for the first time in adult life, usually middle age, is considered to be due to degenerative changes in the wall of the systemic vessel, and is most commonly associated with retro-œsophageal arteries rather than vascular rings. Should this symptom develop then in a case of right-sided cervical aortic arch, the possibility must also be considered that it is due to atheromatous changes in the retro-œsophageal descending part of the aorta—especially when, as in our case, a left-sided ligamentum arteriosum, if present, is probably long and anterior—rather than a ring formation.

King Edward VII
Memorial Chest Hospital,
Hertford Hill, near Warwick. JOHN C. A. RAISON.

5. Tori, G. *Ann. Radiol. diagn., Bologna*, 1948, **20**, 48.
6. *In* Congenital Heart Disease, by J. W. Brown. London, 1950.
7. Wilson, J. C., Warkany, J. *Pediatrics*, 1950, **5**, 708.

Obituary

ANDRIJA STAMPAR

M.D. Vienna

FROM Balkan peasant to first chairman of the Economic and Social Council of the United Nations and president of the first Assembly of the World Health Organisation—such was the record of Andrija Stampar. Like most other men who have made their mark in international health, he first achieved prominence through hard work and advanced ideas in his own country.

Born in 1888 in Croatia, he qualified at Vienna in 1911 and from the beginning showed his abiding interest in social medicine. He wrote and lectured against the evils of alcoholism, and he remained a lifelong teetotaller. After working as a district medical officer in Croatia, he became in 1919 director of public health for the whole of the new kingdom of Yugoslavia in his early thirties and introduced many reforms into the organisation and practice of rural hygiene. In 1931 he returned as professor of hygiene to Zagreb, where a school of public health had been founded with the help of the Rockefeller Foundation. The essence of his teaching was a two-way traffic by which leading villagers came to the school to be taught simple principles which they put into practice on returning home. Such ideas are almost commonplace in underdeveloped rural communities nowadays, but they are only commonplace because of Stampar's initiative and drive.

Dr. Rajchman, director of the Health Organisation of the League of Nations, was among the first to recognise Stampar's work and worth and secured his help for the Health Organisation in various ways, including membership of the Health Committee of the League. He served the League in China from 1933 to 1936 and visited the United States and this country on many occasions. The war—and Stampar's Left-wing views—led to his internment in Austria for a time, but liberation found his beloved Zagreb University, of which he was made rector, intact if impoverished; and he obtained many supplies and books from friends and sympathisers in this and other countries.

Unique among Yugoslavs at that time in his pre-war international experience and reputation, he was quickly restored to even greater international prominence and elected chairman of Ecosoc which, at its first meeting in 1946, acted on the decision of the San Francisco conference that an international conference should be called to consider setting up an international health organisation of the United Nations.

Stampar served on the technical preparatory committee for this international health conference and submitted a memorandum on the constitution of the new agency, besides taking part in the conference itself. It was therefore wholly appropriate that he should have been elected chairman of the Interim Commission of W.H.O. in 1946 and president of its first Assembly in 1948. Since that time until recently he had been associated with the work of W.H.O. in many ways, and in 1955 he received the Leon Bernard Foundation prize for pre-eminent work in social medicine.

A colleague writes:

Stampar's success had three elements—technical competence; political flair; and a peasant toughness which, in the polite world of international health, made men chary of offending him. His very appearance inspired a certain awe. His cannon-ball head, sunk between huge shoulders, looked as if he could batter a breach in a wall with it—sometimes indeed he might have tried to do so to judge from his temper when things had not gone as he wanted! It needed courage, as well as affection, for the chief British delegate to take him by the arm on one such occasion and remark, " Well, you great Balkan bear! How's the sore head this morning? " But all in all he was a great man and his country should be proud of him.

Appointments

DEWAR, A. E., M.B. St. And., F.F.R., D.M.R.D.: assistant radiologist, X-ray diagnostic department, St. Thomas's Hospital, London.

FRANKLAND, A. W., D.M. Oxon.: part-time consultant in charge of the clinic for allergic disorders (Wright Fleming Institute of Microbiology), St. Mary's Hospital, London.

HALL, THOMAS, M.B. Cantab.: assistant M.O., Wembley and Willesden.

MCEVEDY, B. V., M.CH. Oxon., F.R.C.S.: assistant surgeon, Royal Victoria Infirmary, Newcastle upon Tyne, and surgeon, Gateshead hospital group.

MACINTYRE, J. C., M.B. Glasg., D.A.: S.H.M.O. in anæsthetics, Stornoway hospitals.

RHODES, PHILIP, M.B. Cantab., F.R.C.S., M.R.C.O.G.: part-time consultant in obstetrics and gynæcology, St. Thomas's Hospital and Lambeth Hospital, London.

*WILD, A. A., M.B. Edin., D.M.R.D.: full-time consultant in radiology, York A and Tadcaster, Scarborough, Bridlington, Malton and Whitby hospital groups.

Birmingham Regional Hospital Board:

DUNCAN, J. MCK., M.B. Birm., F.R.C.S.: part-time consultant surgeon, Dudley and Stourbridge hospital group.

HOOPER, E. R. S., M.B. Lond., F.F.A.R.C.S., D.A.: part-time consultant anæsthetist, Lichfield, Sutton Coldfield, and Tamworth hospital group.

KALRA, P. L., M.B. Birm., D.P.M.: assistant psychiatrist, St. George's Hospital, Stafford.

PORTER, E. R. D., M.B.E., M.R.C.S., D.P.H.: deputy senior administrative M.O. to the board.

Manchester Regional Hospital Board:

ALLEN, W. M., M.B. Manc., D.M.R.D.: consultant radiologist, Preston and Chorley hospital group.

LEWARS, P. H. D., M.B. Durh., B.D.S.: senior hospital dental officer, South Manchester hospitals.

MARTIN, W. M., M.B. Belf.: assistant anæsthetist, Burnley and district hospital group.

* Amended notice.

Notes and News

EXTENSION TO BIRMINGHAM MENTAL HOSPITAL

ON June 26 Dame Enid Russell-Smith, deputy secretary of the Ministry of Health, opened two 40-bed pavilions at Hollymoor Hospital, near Birmingham.

The new buildings, which are about a quarter of a mile from the main buildings, stand on a southern slope, and have been designed on one floor so that the open outlook from the hospital is unimpaired. The two units are linked by a kitchen with its own service entry. The dayrooms and dining rooms of each unit are next to the kitchen. They have low window sills to make the best use of their southern aspect and view of the Lickey Hills, and open fireplaces of natural clipsham stone. Each unit has two 20-bed dormitories linked by sanitary wings which are also accessible from the day rooms. Light, cheerful colours have been used for walls, door, and curtains, neutral shades for the rubber floors, rugs, and furniture. The scheme was designed by S. N. Cooke and Partners in association with Mr. D. A. Goldfinch, architect to the Birmingham Regional Hospital Board.

After the opening ceremony plaques were unveiled commemorating the work of Dr. S. J. Scurlock, who has lately retired from the post of senior administrative medical officer of the Birmingham regional hospital board, and of Dr. T. A. Lambo, psychiatrist to the Avo Hospital in Western Nigeria, who is cooperating with the hospital in the training of Nigerian student nurses.

ECONOMY IN PRESCRIBING

THE Ministry of Health has accepted the view, expressed in the interim report of the Committee on the Cost of Prescribing,[1] that the supply by executive councils of medical and pharmaceutical lists to drug houses is undesirable. The Ministry has asked any executive councils that hitherto have provided lists in this way to discontinue the practice.

University of Manchester

At recent examinations the following were successful:

M.B., Ch.B.—J. W. Aspinall, Roy Battye, F. H. Brindle, D. B. Brookes, J. E. Brooks, A. L. Buckley, Eric Charles, P. J. Cox, J. S. Cumming, Barry Deakin, B. H. Delany, G. G. Duckworth, R. M. Flinn, Joyce Harris, Roy Haworth, Patricia A. Hegarty, Raymond Holmes, Alexander Hopkins, W. H. Isbister, Maria Z. Kozubowska, R. J. Lawton, I. P. McEwan, A. C. Peterson, J. D. Rhodes, P. H. Roberts, Martin Ryan, Elizabeth M. Spencer, Roy Statham, Garo Tahta, Peter Watson, J. M. Watts, B. K. Wignall, J. D. G. Williams, S. K. Wood, P. B. Wrigglesworth.

D.P.H.—Margaret Armitstead, Horace Bailey, Irene S. Bailey, A. D. Bostock, J. R. Brown, A. S. Dunn, B. R. Ellis, Alexander Gatherer, R. E. Jones, William Lees, Joyce E. Leeson, J. E. Morris, D. W. Preston, Rachel D. R. Sasieni, H. R. Simpson, D. H. Vaughan.

University of St. Andrews

On July 1 the following degrees were conferred:

M.D.—C. C. Booth, J. M. McKenzie, A. P. M. Forrest (with honours); J. O. Forfar (with commendation).

Ch.M.—W. F. Walker (with commendation).

M.B., Ch.B.—F. D. Lee (with honours); I. S. Macmillan, D. N. Grant, Ellen C. G. Tarvit, Harry Ridehalgh, Gordon Wray, J. R. E. Edmondson-Jones (with commendation); J. M. Anderson, Gerald Asbridge, C. W. Avery, Ann Barber, Beatrice M. Catto, Doreen E. Chambers, Hari R. Chandrachud, A. J. W. Clayton, A. R. Cook, Jane M. Cowan, J. N. Cross, D. J. Dallas, A. G. Davies, B. O. Divis, Gerald Donachie, W. H. G. Douglas, W. A. A. Famuyiwa, A. L. Forrest, W. R. Grundy, Valerie L. Gunn, D. M. Hay, M. A. C. Heavens, A. H. Imrie, Yohannes Kebreth, C. D. G. Lewis, A. H. McAdam, Rita A. McIntyre, G. M. Maclure, W. S. McMurray, R. D. Mathias, Eleanor M. Mowat, W. J. Nicol, D. W. Nisbet, Beryl Y. J. Pay, J. L. Penny, T. T. B. Phillips, P. G. C. Robertson, Veronica M. C. Robinson, L. C. Rose, Brigid I. Russell, Natalie A. Sender, Avril J. Smallwood, J. S. Soutar, J. L. Stoller, Soad Tabaqchali.

University of Aberdeen

On July 3 the following degrees were conferred:

M.D.—I. R. Lawson, W. G. D. Murray, C. H. Walker.

Ch.M.—William Burnett (with honours).

M.B., Ch.B.—Kathleen M. R. Chrystal, J. A. Baldwin (with honours); G. A. German, D. G. Jamieson (with commendation); Elizabeth A. Abernethy, J. E. Ashun, Eileen M. Beattie, A. W. S. Brown, R. N. Carter, Anne M. Cluness, J. T. Coull, J. I. Coutts, J. A. Craig, Noreen M. Crookshanks, Geoffrey Dillon, Carol M. Edmond, W. J. W. Freeland, G. A. T. Gill, R. W. Glashan, D. R. Grieve, E. H. Innes, F. K. A. Laing, J. E. Leng, J. G. Lillie, W. S. P. McGregor, J. S. McIntosh, Helen R. McKilligin, R. M. MacLachlan, Sheila C. Martin, Catherine K. Masson, Moira S. Meldrum, A. P. Mowat, A. P. Nicholson, A. G. Nicol, P. P. S. Nylander, James Proudfoot, R. L. Pyle, W. D. Pyle, Jean McC. Ritchie, G. S. Robertson, R. J. Robertson, Isabelle M. Roe, H. J. M. Spicer, G. A. Taylor, John Taylor, R. A. Tozer, Grace C. Turner, A. C. Watt, Jean A. Wright, R. A. Wynter.

D.P.H.—A. G. Beattie, R. F. Blackburn, Fiona J. Lyall, D. M. McLellan, Norman Marshall, T. F. Rennie.

1. See *Lancet*, 1958, i, 1376.

University of Liverpool

At recent examinations the following were successful:

M.D.—B. J. Fairhurst, A. W. Howel-Evans, E. A. Nieman, J. R. Roberts, D. Taylor-Robinson, D. J. West.

Ch.M.—E. C. Edwards, J. H. Y. Fung.

M.B., Ch.B.—R. Harris, Mary B. Jones (with honours); H. M. Alty, A. L. Ansdell, W. K. H. Barnard, J. M. Beresford, G. N. Bhadresa, J. N. Boardman, Mary J. Boardman, M. J. Brindle, A. Broughton, T. N. Calvey, R. P. Christian, P. Cochrane, R. L. Coupe, Marie T. Cox, D. G. Ellis, E. R. Evans, R. E. Fallowfield, R. S. Ford, W. Green, Malvina Harris, J. Higham, L. J. Hipkin, Anne T. Irvine, J. A. Jackson, Anne Jacques, A. W. Jones, D. Jones, E. W. Jones, K. E. Jones, R. H. T. Jones, J. F. Kane, W. E. Kearns, N. B. Kirkland, K. Lilley, W. F. W. E. Logan, H. Martin, Maureen D. Martin, K. Martindale, P. J. Moorhead, Evelyn J. Moss, D. L. Parry, H. J. Phillips, G. H. Prince, P. G. Rae, G. R. Riley, Catherine O. L. Rimington, Aline M. Robertson, R. F. Robertson, C. Roby-Jones, J. M. Romer, Yvonne A. Roope, C. E. Sissons, J. F. Taylor, J. M. Taylor, R. W. Taylor, V. R. Taylor, N. E. Thomas, D. E. Wallace, R. Whitehead, J. G. M. Williams, J. A. Wilson, J. S. Wright, W. D. R. Writer, C. Wynne.

D.P.H.—Sheila I. Angles, Cynthia J. Bladon, P. J. Burke, D. C. Curtin, A. Depares, Cecilia T. Diskin, F. R. Howell, J. V. Loughlin, Anne D. Micah, S. Naylor, J. M. V. Packer, J. A. Seddon, D. Wild.

D.M.R.T.—A. K. Bose, G. A. L. G. Glazebrook, R. Spencer.

D.M.R.D.—Varunee Amatyakul, E. H. Burrows, L. R. Levin, T. Nopparat, R. G. Pitman, H. G. Row.

University of Sheffield

Mr. A. W. Kay, lecturer in surgery in the University of Glasgow, has been appointed to the chair of surgery in succession to Prof. R. P. Jepson.

Mr. Kay, who is 41 years of age, graduated M.B. with honours from the University of Glasgow in 1939. After holding house-appointments in Glasgow at the Western Infirmary and the Royal Hospital for Sick Children, he was appointed in 1941 a Hall tutorial fellow and clinical assistant at the Western Infirmary. In 1942 he took the F.R.C.S.E. and in 1944 he received the degree of M.D. with honours and was awarded the Bellahouston medal. In 1945 he was appointed assistant in the department of surgery at Glasgow University and surgeon to outpatients at the Western Infirmary. After two years as a major in the R.A.M.C., when he was in charge of the surgical division at Millbank Military Hospital, he returned to Glasgow as consultant surgeon to the Western Infirmary and honorary lecturer in surgery at the university. In 1949 he took the CH.M. with honours. In 1955 he became first assistant to Prof. C. F. W. Illingworth, and he was appointed to his present lectureship in 1956. He has also been surgeon in charge of wards at the Western Infirmary since 1956. He is a member of the Medical Research Council's external scientific staff. He was elected F.R.F.P.S. in 1956. Mr. Kay is co-author of a textbook of surgical physiology which is in the press, and his published work includes a paper on the augmented histamine test.

University of Glasgow

On July 5 the following degrees were confered:

M.D.—W. S. Foulds, W. J. Gordon, R. M. H. McMinn, J. T. Naismith, D. D. Smith, H. I. Tankel (with commendation); E. McL. Barbour, J. M. Crawford, J. A. McKinnon.

M.B., Ch.B.—Alastair Ballantyne, J. H. H. Bowie, Margaret C. Donnelly, J. M. Howat, P. H. Pinkerton, R. L. Robinson, J. P. Studzinski, J. K. Todd, Frederick Walker (with commendation); Olúdele da Rocha Afodu, Ahmed Nawaz Ahmad, W. C. Alston, G. K. K. Asamoah, H. D. Baillie, Robert Baird, Maureen E. Barr, R. F. Barr, Isabelle B. Barrie, W. N. Baxter, B. J. Beadsworth, John Bonnar, Dorothy A. Brown, Jean G. Brownlie, K. D. Buchanan, Hellen S. Conn, W. G. Conn, N. A. Coutts, J. E. N. Dickie, Archibald Downie, Bryan Drever, J. C. Drever, Macadam Duncan, J. J. Dunn, J. A. C. Fisher, Adam Fleck, Stewart Fletcher, John Fyfe, Catherine A. Gardner, Joyce O. Garven, R. T. Glen, Robert Gordon, John Gray, K. D. Griffin, Margaret E. Hanlon, W. J. Haran, C. D. Hardie, H. C. Hendrie, Margaret Hennigan, D. M. C. Hislop, Margaret A. Hodson, I. M. Hynd, G. M. Irvine, J. F. St. Clair, Irene M. J. Jackson, J. C. Kellock, M. A. Kelly, Martin Kelvin, Margaret M. Kennedy, H. A. Kilpatrick, I. McA. Kyles, Marjorie M. Langmuir, J. P. Lanz, I. McA. Ledingham, R. E. M. Lees, D. R. H. Lewis, T. I. McBride, J. P. McConnell, D. M. MacDermid, D. M. Macfadyen, D. B. MacGregor, Eileen McGuire, R. L. McKechnie, M. C. MacKenzie, C. A. MacLean, Norman MacLean, R. B. Macleod, G. W. McNicol, Margaret M. Macpherson, J. M. Maguire, J. P. Malone, W. D. Martin, Heather M. May, J. M. B. May, Marie H. H. Mitchell, John Moffat, Jack Murgatroyd, Helen McB. G. Murray, Jean R. Nairn, E. A. Neville, Elizabeth J. Nivison, V. R. Nurse, S. S. I. Parker, K. C. Paton, Mary H. Paul, Andrew Pollock, J. G. Pollock, Janet S. Primrose, A. J. Quigley, A. A. Reid, Daniel Reid, G. L. I. Reilly, Elizabeth M. Riddell, Anthony Rourke, Elizabeth M. Russell, J. L. Russell, Robert Scott, W. S. Scott, M. S. Seltzer, M. G. Sharman, G. R. Sharp, William Simpson, J. F. Smart, Donald Smith, Khodayar Sorooshian, J. C. Spence, A. R. Stewart, T. McC. Stewart, W. B. Stewart, Sheila M. Strachan, M. C. Thomson, J. K. Todd, Maelor Vallance, Alan Vost, Evelyn McD. Walker, J. P. Wall, J. M. Walsh, R. A. Willett, Maureen L. Wyllie, H. N. Young.

University of Dublin

On July 3 at Trinity College, Dublin, the following degrees were conferred:

M.B., B.Ch., B.A.O.—Sara R. Abels, Bridget M. Acheson, H. B. Allen, John Bennett, P. J. Blackburn, J. S. Brown, R. J. M. Collis, Edith M. Cross, N. J. B. De Wet, Bridget A. M. Dunne, Michael Elder, Brian Gallagher, P. B. Galvin, H. G. Grace, Sheila D. Graham, D. E. Jones, Anne Llewellyn, S. H. M. Logan, Patricia M. Norman, John Quinn, Joan Richards, Annette L. K. Roberts, P. J. Robinson, W. M. Robinson, Lorna J. Rust, Pauline E. Tan, D. G. Weir, T. D. H. Wilson, Theodore Winston, Susan E. J. Young.

M.D.—T. H. Bewley, F. O. Dosekun, Edna La C. Murphy.

M.A.O.—C. J. B. Orr.

Royal College of Surgeons of England

On July 3, Mr. Eric Riches and Sir Arthur Porritt were re-elected, and Mr. F. W. Holdsworth and Mr. J. Cridlan Barrett were elected members of the council.

Order of St. John of Jerusalem

The Queen has sanctioned the following promotions in, and appointments to, this order:

As Knights.—Colonel F. A. Bearn, C.B.E., D.S.O., M.C., M.D., H. S. Taylor-Young, F.R.C.S.

As Commanders.—Major-General A. E. Campbell, C.B., M.D., Q.H.P., Colonel Malcolm MacEwan, D.S.O., O.B.E., D.F.C., T.D., M.B., Surgeon Rear-Admiral D. M. Beaton, O.B.E., L.R.C.P.E., Q.H.P., Surgeon Rear-Admiral D. F. Walsh, O.B.E., F.R.C.S.E., E. C. Brewis, M.D., T. W. A. Gray, M.D., Colonel G. E. Wight, O.B.E., M.D., Elsie C. Hanson, M.D.

As Officers.—Major-General T. F. M. Woods, O.B.E., M.D., Q.H.P., Lieut.-Colonel D. H. D. Burbridge, M.R.C.S., J. B. Dobson, F.R.C.S., A. D. Griffith, L.M.S.S.A., Archibald Russell, M.B., D. P. Kennedy, B.D., M.B., J. G. Stewart, M.C., M.B., T. H. Pullar, M.R.C.P., James Moffat, M.B., W. A. Hogg, M.B., H. J. Hoby, M.R.C.S., L. S. Potter, M.B., Colonel Geoffrey Anderton, O.B.E., M.B., F. E. Fletcher, M.R.C.P., J. W. Pickles, M.B., C. D. Short, M.D., Brigadier C. S. Thompson, O.B.E., M.D., M. G. Townsend, M.D., Marguerite F. E. Wyile, M.R.C.S.

Society of Apothecaries of London

On July 22, at 8.30 P.M. at the hall of this society, Black Friars Lane, E.C.4, the Master will confer the honorary freedom of the society on Sir Henry Souttar and bestow the Galen medal on Sir Macfarlane Burnet.

Royal Society of Medicine

The following officers have been elected for 1958–59:

President, Sir Geoffrey Marshall; immediate past president, Sir Clement Price Thomas; hon. treasurers, Mr. E. G. Muir and Dr. Basil Kiernander; hon. secretaries, Mr. Terence Cawthorne and Prof. R. H. S. Thompson; hon. librarians, Prof. C. G. Rob and Dr. J. S. Richardson; hon. editors, Dr. E. C. Warner and Mr. Selwyn Taylor; hon. directors of photography, Mr. Myles Formby and Dr. F. C. Kelly.

Institute of Diseases of the Chest, London

Clinical demonstrations, open to doctors without fee, will be continued at this institute (in the grounds of the Brompton Hospital, Fulham Road, S.W.3) on Fridays at 5 P.M. throughout the summer.

Royal Society

With awards from the society's Nuffield Foundation Commonwealth bursaries scheme, Prof. T. Gilman (Natal) is to study skin regeneration at University College, London, and Dr. T. B. Teoh (Hong Kong) bile thrombi at University College Hospital Medical School.

Royal Medical Benevolent Fund

The annual general meeting of this Fund is to be held on Wednesday, July 30, at 5 P.M. at 11, Chandos Street, London, W.1.

Anglo-French Bursaries

Awards have been made for work in France in 1958 under the exchange arranged by the Institut National d'Hygiène, Paris, and the Ciba Foundation, London, to Dr. Evan Fletcher, Dr. J. G. Howard, Dr. E. M. Jepson, Mr. J. F. O. Mitchell, and Dr. P. M. Peacock.

Harveian Society of London

Members of this society on June 22 attended a service at Hempstead Church, Essex, where William Harvey is buried. Lessons were read by Dr. D. A. Imrie, president of the society, and Mr. A. Dickson Wright, president of the Harvey Tercentenary Congress, and the Bishop of Colchester preached the sermon. The appeal fund for restoration of the church tower has now reached over £3000.

International Congress of Psychotherapy

This congress will be held in Barcelona from Sept. 1 to 7. Application to take part should be made to the secretary, Catedra de Psiquiatria de la Facultad de Medicina, Casanova 143, Barcelona. There will be a special section on psychopharmacology, details of which may be had from Prof. F. G. Valdecasas, department of pharmacology of the faculty. Applications must be submitted not later than July 31.

British Association of Paediatric Surgeons

This association will hold its annual meeting in London from Wednesday, July 23, to Friday, July 25.

International Congress on Nutrition

This congress will be held in Washington from Sept. 1 to 7, 1960. Further particulars may be had from Dr. M. O. Lee, 9650, Wisconsin Avenue, Washington 14, D.C., U.S.A.

Health Services Whitley Council

The council have appointed Sir William Matthews, a former under-secretary at the Treasury, and Mr. R. E. Peers, assistant secretary of King Edward's Hospital Fund for London, to join Sir Noel Hall on a committee to compare the wages of National Health Service workers with those of people in similar employment.

Changes in the Prescribed Diseases Schedule

The Minister of Pensions and National Insurance has made regulations (S.I. 1958, no. 1068) altering the schedule of occupational diseases for which workers are covered for the benefits of the Industrial Injuries Act. The regulations implement the recent recommendations of the Industrial Injuries Advisory Council (see *Lancet*, 1958, i, 906).

Progress in the Biological Sciences in Relation to Dermatology

A course on this subject will be held by the University of Cambridge Postgraduate Medical School from Sept. 22 to 27.

It will consist of half-day sessions, each devoted to a group of papers on the same or related subjects, including the melanocyte and melanogenesis, cutaneous innervation, the histochemical investigation of the skin, bacteriology, psychophysiological mechanisms, comparative medicine, immunology, inflammation, carcinogenesis, radiation of the skin, and pharmacology. The course is designed for dermatologists but is open to any doctor interested in the subjects under discussion. Accommodation and board will be provided in Downing College. Further particulars may be had from the secretary of the Medical School, Tennis Court Road, Cambridge.

On July 3 at the Middlesex Hospital Medical School Lord Astor of Hever presented the Comfort Crookshank medal to Prof. Charles Huggins of Chicago.

List of Films on Human Anatomy and Embryology.—In preparing the second edition of this world list Dr. R. Brouwer has found it necessary to limit the number of films selected. Some films showing the anatomy or embryology of animals have been omitted, but others dealing with human anatomy and embryology have been added. Copies (£1) are available from the Netherlands Scientific Film Association, Catharijnesingel 59, Ingang Sterrenbos, Utrecht, Holland.

Diary of the Week

JULY 13 TO 19

Monday, 14th

GUY'S HOSPITAL MEDICAL SCHOOL, London Bridge, S.E.1
5 P.M. Prof. Alfred Jost: Biological Basis of Some Recent Concepts about Sex. (Addison lecture.)

Tuesday, 15th

UNIVERSITY OF LONDON
5 P.M. (St. Thomas's Hospital Medical School, S.E.1.) Dr. Frank Gerbode (San Francisco): Aspects of Intracardiac Surgery.

BRITISH MEDICAL ASSOCIATION
3 P.M. *With the Association of Industrial Medical Officers.* (Portland Building, Nottingham University.) Dr. Andrew Meiklejohn: Industrial Health—Meeting the Challenge. (Mackenzie Industrial Health lecture.)

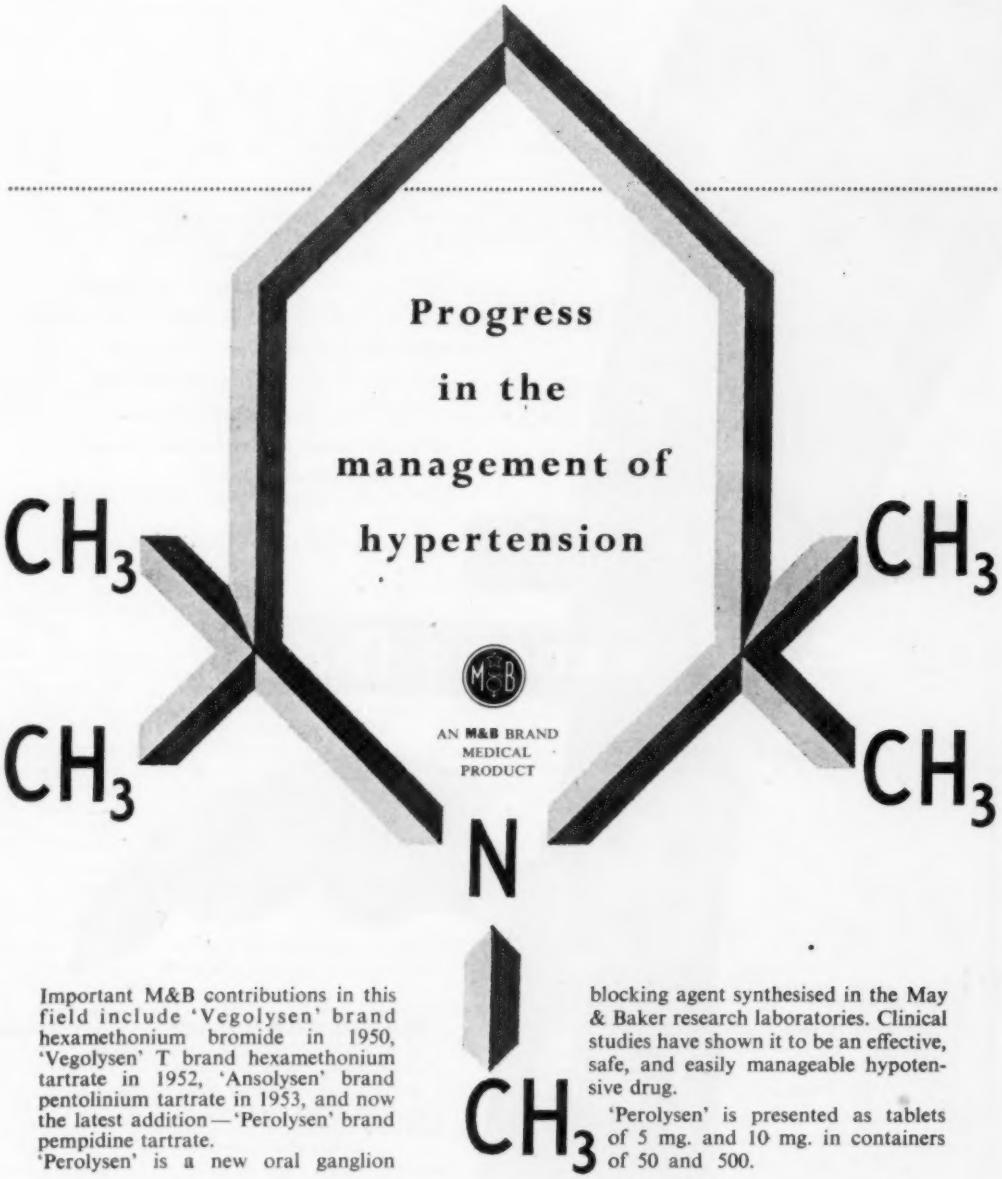
ROYAL COLLEGE OF SURGEONS OF EDINBURGH, 18, Nicolson Street, Edinburgh, 8
3.30 P.M. Prof. I. S. Ravdin (Philadelphia): Recent Advances in Blood-transfusion.

Wednesday, 16th

POSTGRADUATE MEDICAL SCHOOL, Ducane Road, W.12
2 P.M. Dr. A. C. Cunliffe: Cutaneous Hypersensitivity.

Friday, 18th

ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn Fields, W.C.2
4 P.M. Prof. H. G. Radden: Local Factors in Healing of the Alveolar Tissues. (Charles Tomes lecture.)



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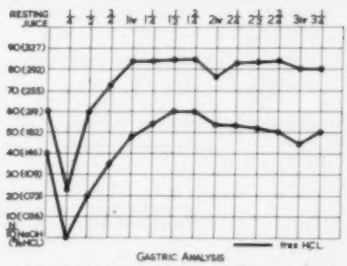
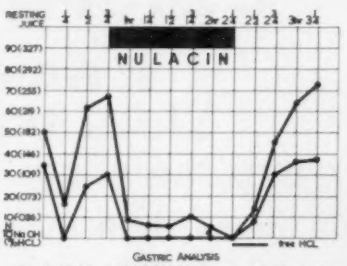


GASTRIC ANALYSIS *Superimposed gruel fractional test-meal curves of five cases of duodenal ulcer.*

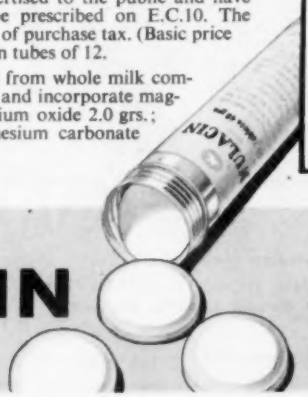


GASTRIC ANALYSIS *Same patients as in Fig. 1, two days later, showing the striking neutralizing effect of sucking Nulacin tablets (3 an hour). Note the return of acidity when Nulacin is discontinued.*

BIBLIOGRAPHY

Practitioner, 1957, **178:** 43
Practitioner, 1956, **176:** 103
Amer. J. Gastro. 1956, **26:** 665
Brit. Med. J. 1954, **1:** 46

Further references to the literature and full information on Nulacin available on request.



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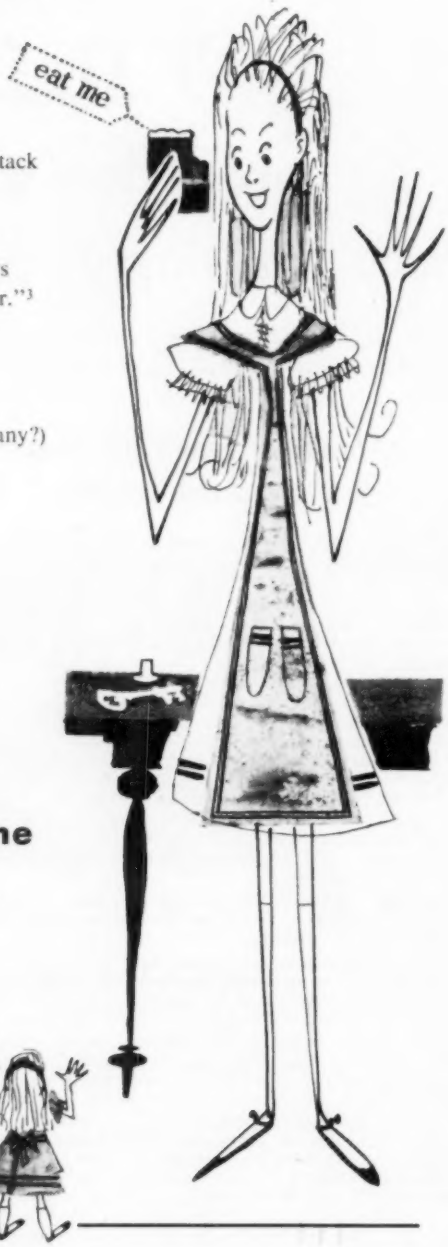
[1] *J. nerv. ment. Dis.* (1952) **116**, 346 [2] *Lancet* (1956) **1**, 794
[3] *Canad. med. Ass. J.* (1955) **73**, 701



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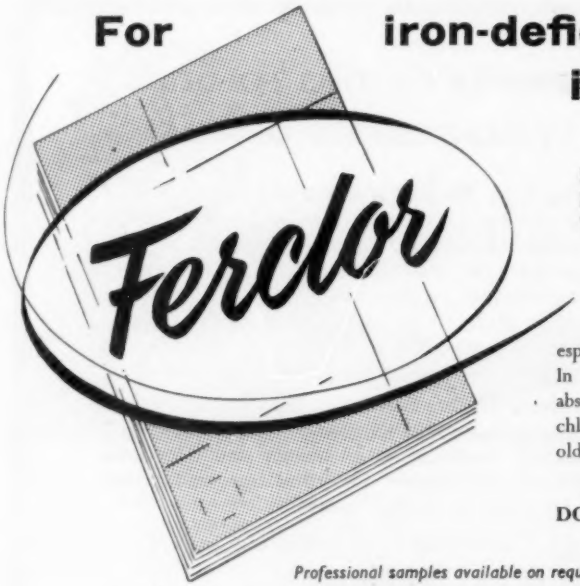

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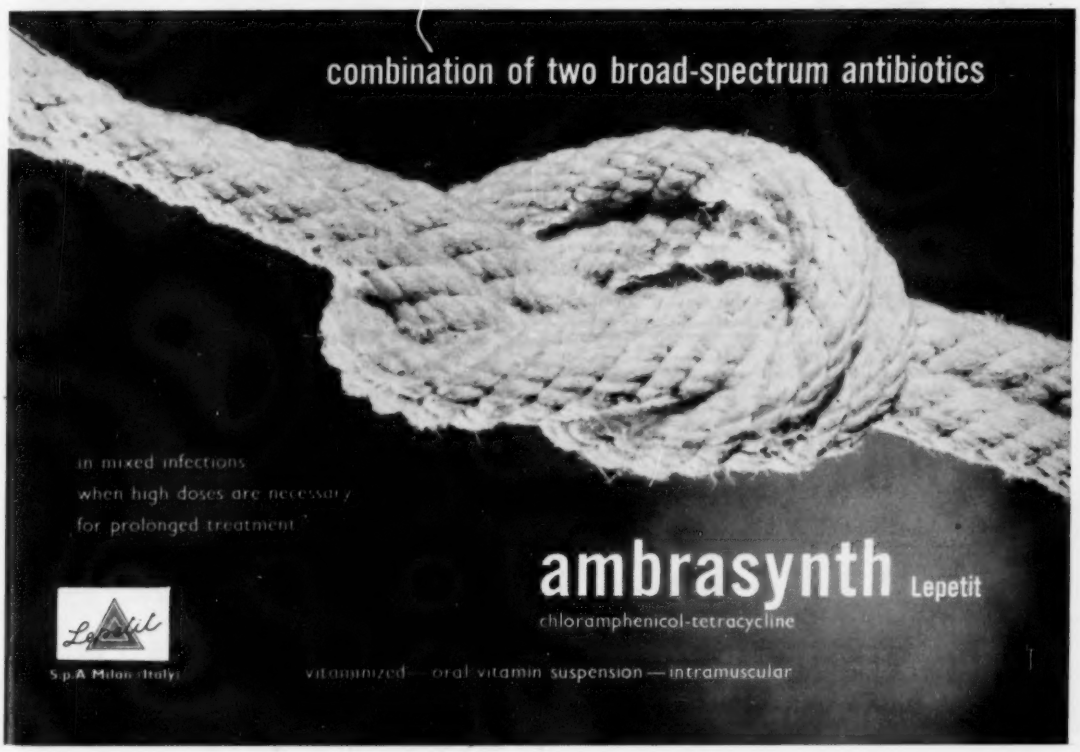

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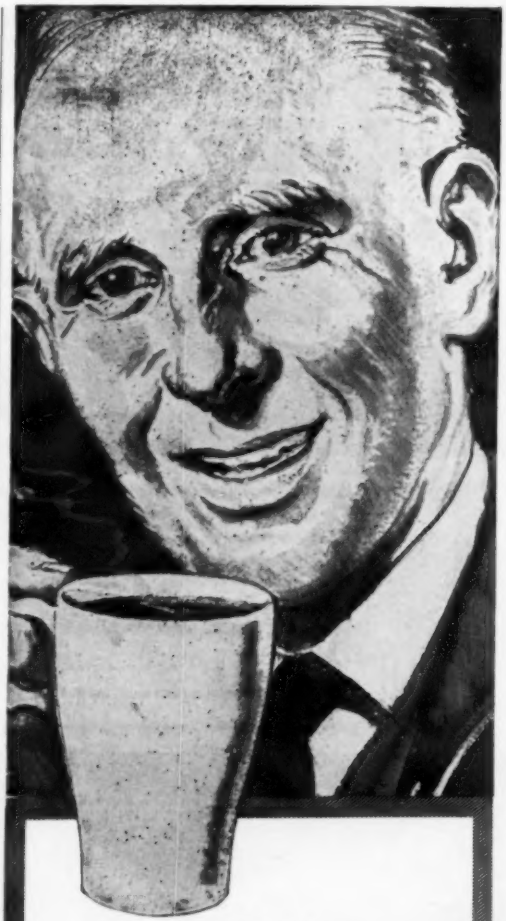

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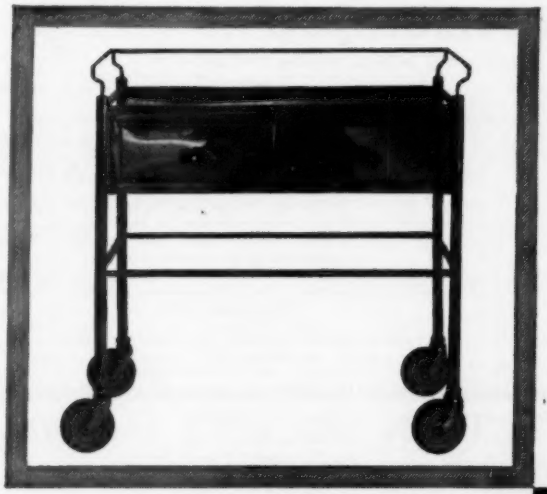

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The Terms and Conditions of Service of Hospital Medical and Dental Staff apply to all N.H.S. hospital posts we advertise, unless otherwise stated. Canvassing disqualifies, but candidates may normally visit the hospital by appointment.

Academic and Educational

ROYAL COLLEGE OF PHYSICIANS

LEVERHULME RESEARCH SCHOLAR

Applications are invited for a Leverhulme Research Scholarship value of £1000 a year. The Scholarship will be for 1 year in the first instance and may be renewed for a maximum of 3 years. A scholar must satisfy the College that the major part of his time is spent on his research but he may be allowed to hold another appointment. Scholars must devote themselves to the investigation of some problem related to disease as it occurs in man, in any branch of medicine. The work must be done in some established institution, preferably in the United Kingdom, in which full facilities for the research are available.

Applications, accompanied by the names of 2 referees, should state details of the proposed work, the name of the individual under whom it is proposed to work, and the Institution where the work is to be done. Application forms may be obtained from the Assistant Registrar, Royal College of Physicians, Pall Mall East, London, S.W.1. Applications for the Scholarship must be received not later than 29th September, 1958.

THE UNIVERSITY and the ROYAL FACULTY OF PHYSICIANS AND SURGEONS OF GLASGOW

POST-GRADUATE MEDICAL EDUCATION COMMITTEE

PRIMARY EXAMINATION FOR THE SURGICAL FELLOWSHIPS OR FOR THE F.F.A. R.C.S.

A COURSE OF INSTRUCTION in Anatomy, Physiology, Biochemistry, Pathology and Bacteriology suitable for candidates preparing for the Primary Examination of the Fellowship *qua* Surgeon of the Royal Faculty of Physicians and Surgeons of Glasgow will be held from 6TH OCTOBER to 5TH DECEMBER, 1958. (The Primary Examination conducted by the Glasgow Royal Faculty is accepted by the Royal College of Surgeons of Edinburgh, of England, and in Ireland in lieu of the corresponding examinations of these Bodies).

The Course will comprise a total of approximately 180 hours' instruction given daily from Mondays to Fridays, between the hours of 12 NOON and 5.30 P.M.

The Course will be open to junior staff of hospitals in the Western Region of Scotland and also to other suitable applicants. Applicants not employed in the hospitals of the Western Region may, if they wish, be given an honorary clinical attachment to one of the surgical teaching units.

The fee for the Course is £30.

A modified form of the Course is available for trainees in Anæsthetics. This modified Course will provide 9 weekly sessions on the pharmacology of the anæsthetic drugs in place of the sessions on embryology in the surgical Course.

Trainees in anæsthetics who are unable to take the complete Course may enrol for the Pharmacology Course alone at a fee of £6.

For further details and syllabus of the Course, application should be made to the Director of Post-Graduate Medical Education, The University, Glasgow, W.2.

THE MILROY LECTURES ON STATE MEDICINE AND PUBLIC HEALTH

The Council of the Royal College of Physicians of London are prepared to receive applications for the office of MILROY LECTURER for 1960.

Applications must be addressed to the Registrar, Royal College of Physicians, Pall Mall East, S.W.1, to reach the College on or before Wednesday, 10th September, 1958, and to include a short synopsis of the subject selected by the candidate.

2 lectures are to be given on a Tuesday and Thursday in February or March, 1960.

A copy of Dr. Milroy's "Suggestions" on the subject of his bequest, and information as to the emolument, may be obtained from the Registrar.

TANCRED'S STUDENTSHIPS

DIVINITY : MEDICINE : LAW

£100 p.a. each. For men only

The Governors and Trustees of Tancred's Foundation propose to make their annual election of a Student in Physic at Gonville and Caius College, Cambridge, on the result of the Entrance Examination to be held in January, 1959, required from candidates for admission to Gonville and Caius College, Cambridge, who intend to read medicine.

Candidates must have been born in England, Scotland or Wales and be members of the Church of England and unmarried. Candidates must be within the ages of 17 years and 22 years on 1st October, 1959. The last day for sending in Petitions is 1st October, 1958.

Further announcements relating to the Divinity and Law Studentships awarded by this Foundation will appear in September, 1958, and February, 1959.

Apply for further particulars and form of Petition stating kind of Studentship and mentioning this paper to the Clerk, Tancred's Foundation, 28, Lincoln's Inn-fields, London, W.C.2.

GLASGOW POSTGRADUATE MEDICAL EDUCATION COMMITTEE

COURSE IN MENTAL DEFICIENCY

A short intensive Postgraduate Course in Mental Deficiency will be held from 6TH OCTOBER to 24TH OCTOBER, 1958.

The Course will comprise:

(*a*) Lectures and demonstrations in various aspects of mental handicap and mental deficiency;

(*b*) Instruction in mental testing;

(*c*) Visits to institutions.

Fee: £18.

The Course will be limited to 20 practitioners, places being allocated in order of return of application forms, which may be obtained from the Director of Postgraduate Medical Education, The University, Glasgow, W.2.

GLASGOW POST-GRADUATE MEDICAL EDUCATION COMMITTEE

COURSE IN THE PRINCIPLES AND APPLICATION OF CHEMOTHERAPY IN ACUTE AND CHRONIC INFECTIOUS DISEASE

RUCHILL HOSPITAL: 4–5TH OCTOBER, 1958

This short 2-day Course on the principles and application of chemotherapy in acute and chronic infections has been arranged to suit the convenience of general practitioners who might find it inconvenient to take a longer period away from their practice.

On each day, classes will run from 9 A.M. until 5 P.M., and the teaching will be in the form of lectures, lecture demonstrations, seminar discussions and demonstrations of laboratory practice.

The Course is intended to give within a short period a comprehensive and up-to-date description of the forms of chemotherapy in common use and their best methods of administration.

The fee for the Course is 2 guineas.

National Health Service practitioners may, subject to certain conditions, obtain the fee and restricted travelling and subsistence expenses from Government sources.

Since the number of places is limited, those wishing to attend should make early application to the Director of Post-Graduate Medical Education, The University, Glasgow, W.2, from whom further information may be obtained.

GLASGOW ROYAL INFIRMARY

MCINTYRE CLINICAL RESEARCH SCHOLARSHIP

Applications are invited from young medical men for the above scholarship. The work of this scholarship may be devoted to any branch of clinical investigation. The appointment is whole-time and remuneration is at the rate of £750 p.a.

Applications should be forwarded, with the names of not more than 3 referees, to the undersigned, from whom further particulars may be obtained.

J. KILLOCH ANDERSON, Medical Superintendent.

L.M.S.S.A.

FINAL EXAMINATION: MEDICINE and SURGERY, 11th August, 13th October, 10th November, 1958. MIDWIFERY and PATHOLOGY, 12th August, 14th, October, 11th November, 1958. MASTERY OF MIDWIFERY, May and November. DIPLOMA in INDUSTRIAL HEALTH, July and December.

For regulations apply REGISTRAR, Apothecaries Hall, Black Friars-lane, London, E.C.4.

UNIVERSITY OF CAMBRIDGE

PINSENT-DARWIN STUDENTSHIP

The Managers hope shortly to elect for 1 year in the first instance to a STUDENTSHIP IN MENTAL PATHOLOGY of the value of £700. The student must engage in original research into any problem having a bearing on mental disorder or defect.

Applicants should write before 28th July to the Secretary, Pinsent-Darwin Studentship, Department of Medicine, Tennis Court-road, Cambridge, stating their age and qualifications and the general nature of the research that they wish to undertake.

GUY'S HOSPITAL. It is proposed to appoint a Research FELLOW to investigate the incidence of staphylococci in relation to the frequency of cross-infection in hospitals. Applicants should be medically qualified and of Registrar or possibly Senior Registrar status. They should have an interest in laboratory methods and preferably considerable bacteriological experience. The appointment would be for 1 year in the first instance, commencing on or before 1st October, 1958.

Application should be made by 19th July, 1958, on a form obtainable from the Dean, Guy's Hospital Medical School, S.E.1.

GUY'S HOSPITAL MEDICAL SCHOOL, London Bridge, S.E.1. Applications are invited for a Full-time RESEARCH FELLOWSHIP in the Thoracic Surgical Unit for Research on Cardiovascular problems. It is desirable that applicants should possess a higher qualification in surgery. Initial salary normally within the range £935–£1210 p.a., according to the experience and qualifications of the person appointed, but in special circumstances a higher initial salary would be considered.

Applications, with the names of 3 referees, should be sent to the Dean by 26th July, 1958.

ROYAL FREE HOSPITAL SCHOOL OF MEDICINE, Hunter-street, London, W.C.1. Applications are invited from registered medical practitioners (Men or Women) for appointment as LECTURER IN CHEMICAL PATHOLOGY from 1st October, 1958. The Lecturer is also Honorary Assistant Chemical Pathologist to Royal Free Hospital; duties include teaching, research and hospital diagnostic routine. Previous general experience in pathology essential. Salary £1150–£100–£1750 p.a., with superannuation benefits and family allowances.

Applications (7 copies), with names of 2 referees, not later than 6th August, 1958, to Secretary at above address, from whom further particulars may be obtained.

UNIVERSITY OF CAMBRIDGE. Department of Medicine. Applications are invited for the post of ASSISTANT IN RESEARCH IN MEDICAL PSYCHOLOGY, to begin duties on 1st October, 1958, or as soon as possible thereafter. The person appointed, who should have a registered medical qualification, will be required to engage in clinical and experimental research under the direction of the Reader in Medical Psychology. Pensionable stipend is on the scale £650–£25–£850, the appointment being for a year in the first instance.

Further information may be obtained from Dr. D. A. GRESHAM, Secretary of the Appointments Committee of the Faculty of Medicine, The Medical School, Tennis Court-road, Cambridge, to whom candidates should send 10 copies of their application, with the names of not more than 3 referees, to reach him not later than 28th July, 1958.

EDINBURGH UNIVERSITY GENERAL PRACTICE TEACHING UNIT. There will be a vacancy in this Unit for a TRAINEE ASSISTANT under the conditions of the National Health Service Acts, with effect from 1st October, 1958.

Applicants should submit full particulars to the Director, Edinburgh University General Practice Teaching Unit, 39, Cowgate, Edinburgh, not later than 30th August, 1958.

EDINBURGH UNIVERSITY GENERAL PRACTICE TEACHING UNIT. This Unit is carrying out a detailed job analysis and morbidity study of the work of a combined practice comprising 5000 patients. A medically qualified RESEARCH ASSISTANT is required for a period of 1 year, beginning 1st October, 1958. The salary will be at the rate of £1000 p.a. As well as carrying out specific duties under the supervision of the Director, the successful applicant will be given the opportunity of studying both the teaching and research methods employed in the Unit. Preference will be given to applicants having previous experience of general practice.

Applications, giving full particulars, should be sent to the Director, Edinburgh University General Practice Teaching Unit, 39, Cowgate, Edinburgh, not later than 1st August, 1958.

UNIVERSITY OF DURHAM. King's College, Newcastle UPON TYNE. DEPARTMENT OF PHYSIOLOGY. The Council of King's College invite applications for the post of DEMONSTRATOR IN PHYSIOLOGY. The Demonstrator will be concerned chiefly with the teaching of dental students. The appointment will be for 1 year in the first instance but renewable up to a maximum of 3 years. The salary ranges are as follows :—

Medical: £700–£1000.
Non-medical: under 26 £650–£700,
over 26 £700–£750.

There are annual increments of £100 for medical and £25 for non-medical demonstrators.

Applications (12 copies), together with the names of 3 persons to whom reference may be made, should be submitted not later than 6th August, 1958, to the undersigned, from whom further particulars may be obtained.

G. R. HANSON, Registrar of King's College.

THE UNIVERSITY OF LIVERPOOL. Applications are invited for the post of ASSISTANT LECTURER in the Department of Physiology : from medically qualified candidates, salary range £900–£1100 p.a. ; or from non-medically qualified candidates, salary range £700–£850 p.a.

Applications, stating age, academic qualifications and experience, should be received not later than 26th July, 1958, by the Registrar, from whom further particulars of the conditions of appointment may be obtained.

THE WELSH NATIONAL SCHOOL OF MEDICINE. Applications are invited for the appointment of LECTURER (full-time) in the Professorial Medical Unit, for a period of 2 years in the first instance. Salary will be in the range £900–£1050–£1750 p.a., but this scale is now under review. Commencing salary will be according to age, qualifications and experience, with participation in superannuation and family allowance schemes.

Further particulars of the appointment may be obtained from the undersigned, by whom applications should be received within 3 weeks of the appearance of this advertisement.

34, Newport-road, Cardiff. F. DODSWORTH, Secretary.

THE QUEEN'S UNIVERSITY OF BELFAST invites applications for a LECTURESHIP IN THERAPEUTICS AND PHARMACOLOGY from 1st January, 1959, or such other date as may be arranged. The salary will be in the range £1300–£50–£2100, with provisions for superannuation. Initial placing on the salary scale will depend upon experience and qualifications. In certain circumstances the salary may rise to £2550. A special interest in and experience of problems of chest diseases would be desirable.

Applications should be submitted not later than 8th September, 1958. Further particulars may be obtained from G. R. COWIE, M.A., LL.B., J.P., Secretary.

KANEMATSU MEMORIAL INSTITUTE OF PATHOLOGY. Applications are invited from qualified medical practitioners for the position of DIRECTOR at a commencing salary of £3616 (Australian currency), including £100 as remuneration for administrative duties. The duties of the Director are mainly to devote himself to his chosen field of medical research. He will also be expected to exercise general supervision over the routine work of the Institute.

Further particulars, set out in a brochure and the 1956 annual report of the Institute, may be obtained from the Editor, THE LANCET, 7, Adam-street, Adelphi, London, W.C.2. Superannuation: Contributory scheme available after completing 1 year's service.

Applications, with copies of published papers, should reach the President, Sydney Hospital, Sydney, New South Wales, Australia, not later than 30th September, 1958.

6th June, 1958. E. C. DOCKING, Secretary.

UNIVERSITY COLLEGE, Ibadan, Nigeria. Applications are invited for LECTURESHIP IN ANÆSTHETICS. Initial appointment 3 years. Salary scale £1700–£100–£2100 p.a. Post carries honorary appointment as Consultant to University College Hospital. Passages paid for appointee, wife, and 3 children under 11 years, on appointment, annual overseas leave and termination. Children's, car and outfit allowances. F.S.S.U. Part-furnished accommodation.

Detailed applications (10 copies), naming 3 referees, by 18th August, 1958, to Secretary, Senate Committee on Colleges Overseas in Special Relation, University of London, Senate House, London, W.C.1, from whom further particulars may be obtained.

AUSTRALIA. UNIVERSITY OF SYDNEY. Applications are invited for the position of SENIOR LECTURESHIP IN MEDICINE. Salary for a Senior Lecturer is within the range £A2200–£A80–£A2550 p.a., plus cost-of-living adjustment, and will be subject to deductions under the State Superannuation Act. The commencing salary will be fixed according to the qualifications and experience of the successful applicant. Under the Staff Members' Housing Scheme in cases approved by the University and its Bankers, married men may be assisted by loans to purchase a house.

Further particulars and information as to the method of application may be obtained from the Secretary, Association of Universities of the British Commonwealth, 36, Gordon-square, London, W.C.1. The closing date for the receipt of applications, in Australia and London, is 30th September, 1958.

AUSTRALIA. UNIVERSITY OF SYDNEY. Applications are invited for a SENIOR RESEARCH FELLOWSHIP in the Department of Surgery. The Appointment will be for 3 years in the first instance. The salary will be within the range £A2500–£3000 p.a. depending on the qualifications of the successful candidate. The work will be conducted in the laboratories of the Department of Surgery and will be concerned with the physiological or biochemical basis of surgery depending upon the training and interests of the appointee. The facilities of the professorial wards of the Royal Prince Alfred Hospital will be freely available for any investigations requiring clinical material.

Applications, stating qualifications and giving the names of 2 referees, should be sent in writing to the undersigned before 30th September, 1958. In addition, overseas candidates are required to forward a copy of the application to the Secretary, Association of Universities of the British Commonwealth, 36, Gordon-square, London, W.C.1, by the same date.

Further information may be obtained from the Professor of Surgery. M. A. TELFER, Registrar, University of Sydney, Sydney, New South Wales, Australia.

UNIVERSITY OF WESTERN AUSTRALIA. Applications are invited for the position of LECTURESHIP IN MICROBIOLOGY. The salary range for Lecturers at present is £A1550–£2050 p.a. for a Science graduate, and £A1650–£2150 p.a. for a Medical graduate. The commencing salary will be determined on the basis of the qualifications and experience of the appointee. An allowance is made towards travelling expenses, and housing assistance is available.

Further particulars and information as to the method of application may be obtained from the Secretary, Association of Universities of the British Commonwealth, 36, Gordon-square, London, W.C.1. The closing date for the receipt of applications, in Australia and London, is 8th September, 1958.

Hospital Services: Senior Appointments

HOSPITALS FOR DISEASES OF THE CHEST. Board OF GOVERNORS. Applications are invited for the post of RESEARCH BACTERIOLOGIST for work particularly concerned with the chemotherapy of tuberculosis. Applicants should possess a medical degree and sound experience of bacteriology methods. The appointment is for 1 year in the first instance, renewable for 1 further year. Salary £1653 15s.–£52 10s.–£2126 5s. p.a.

Applications by 9th August, 1958, to KENNETH A. F. MILES, Secretary to the Board, Brompton Hospital, S.W.3.

NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD.

(1) CONSULTANT PSYCHIATRIST, 3 half-days a week, British Hospital for Functional Nervous Disorders, 72, Camden-road, N.W.1.

Applications before 15th August, 1958.

(2) CONSULTANT ANÆSTHETIST, whole-time or maximum sessions, Whittington Hospital, Highgate-hill, N.19 (1081 Beds).

Applications before 11th August, 1958.

Hospitals may be visited by direct appointment.

Application forms obtainable from and returnable to Secretary, North West Metropolitan Regional Hospital Board, 11A, Portland-place, W.1.

BIRMINGHAM REGIONAL HOSPITAL BOARD. Part-time CONSULTANT RADIOLOGIST (9 notional half-days weekly). Duties mainly in Coventry and Nuneaton. Wide experience specialty and higher qualification essential. Knowledge of vascular radiology desirable.

Applications (15 copies), stating age, qualifications, nationality, present and previous appointments and details of 3 referees, to Secretary, 10, Augustus-road, Birmingham, 15, by 11th August, 1958.

EAST ANGLIAN REGIONAL HOSPITAL BOARD. ASSISTANT DENTAL SURGEON (whole-time), Ipswich and East Suffolk Area. Duties include participation in outpatient and operating sessions at Ipswich and East Suffolk Hospital and inpatient work in chest, mental, and long-stay hospitals in the area. Wide experience in specialty and higher qualifications necessary. Salary scale £1653 15s.–£2126 5s.

Applications (8 copies), stating age, experience and the names of 3 referees, to Board's Senior Administrative Medical Officer, 117, Chesterton-road, Cambridge, by 5th August, 1958. Candidates invited to visit by direct arrangement with Hospital Management Committee Secretary, Ipswich and East Suffolk Hospital, Anglesea-road Wing, Ipswich.

EAST ANGLIAN REGIONAL HOSPITAL BOARD. CONSULTANT OBSTETRICIAN AND GYNÆCOLOGIST (part-time for equivalent of 4 notional half-days weekly) at Great Yarmouth and Lowestoft Hospitals. The successful candidate will be required to reside in or near Great Yarmouth. Wide experience and higher qualifications essential.

Applications (8 copies), stating age, experience and names of 3 referees, to Board's Senior Administrative Medical Officer, 117, Chesterton-road, Cambridge, by 4th August, 1958. Candidates invited to visit Hospitals by direct arrangement with Hospital Management Committee Secretary, Norfolk and Norwich Hospital, Norwich.

LEEDS REGIONAL HOSPITAL BOARD. Senior Casualty OFFICER (whole-time) for duties at the Royal Halifax Infirmary. The appointment will include duties in casualty and orthopædic surgery at the above Hospital with associated ward and operating duties under the general supervision of the Consultant in charge. The person appointed will be required to reside in Halifax. The salary will be within the range of £1653 15s.–£2126 5s. p.a. and the tenure of the post will be for a period not exceeding 4 years.

Applications (12 copies), stating age, qualifications, details of appointments held, showing dates, with names and addresses of 3 referees, to the Secretary, Park-parade, Harrogate, by 7th August, 1958.

LINGFIELD HOSPITAL SCHOOL FOR EPILEPTIC CHILDREN. Applications are invited for the post of DEPUTY MEDICAL SUPERINTENDENT. Neurological or paediatric experience desirable. Mainly medical but some administrative duties. Salary according to the scale for Senior Hospital Medical Officers. A house is available at a nominal rent for a married man. Superannuable under F.S.S.N., to which pension rights are transferable.

Applications, stating age, marital status, full particulars of qualifications and experience and names of 2 referees, to be sent to the Medical Superintendent, Lingfield Hospital School, Lingfield, Surrey.

LIVERPOOL REGIONAL HOSPITAL BOARD. Whiston AND RAINHILL HOSPITALS. Applications are invited for the post of CONSULTANT PATHOLOGIST (whole-time or maximum part-time sessions) with duties at the above Hospitals. Applicants should possess a higher qualification and should have at least 5 years' experience in clinical pathology including at least 3 years in hospital pathology.

Forms of application from Dr. T. Lloyd Hughes, Senior Administrative Medical Officer, Liverpool Regional Hospital Board, 19, James-street, Liverpool, 2, to be returned not later than 26th July, 1958.

VINCENT COLLINGE, Secretary to the Board.

LIVERPOOL REGIONAL HOSPITAL BOARD. Applications are invited for the following 2 posts of Part-time CONSULTANT OTORHINOLARYNGOLOGIST.

(*a*) Mainly at hospitals in the St. Helens, Warrington, Ormskirk and Runcorn areas with some duties in the adjacent areas of Lancashire—7 notional half-days.

(*b*) Mainly at Clatterbridge Hospital with some duties at other hospitals in the Wirral area—5 notional half-days.

Applications are also invited for the post of ASSISTANT OTORHINOLARYNGOLOGIST (Consultant) for 2 notional half-days at Bootle, Walton and John Bagot Hospitals. The duties will be mainly at Bootle Hospital, and the person appointed will apportion his time at the other hospitals under the direction of the Senior Consultant in the Group.

Applicants should possess a higher qualification in surgery and have wide experience in E.N.T. surgery.

Forms of application from Dr. T. Lloyd Hughes, Senior Administrative Medical Officer, Liverpool Regional Hospital Board, 19, James-street, Liverpool, 2, to be returned not later than 26th July, 1958.

VINCENT COLLINGE, Secretary to the Board.

LIVERPOOL. THE UNITED LIVERPOOL HOSPITALS. Applications are invited for appointment as CONSULTANT OTORHINOLARYNGOLOGIST of Junior status for duty initially at the Liverpool Ear, Nose and Throat Infirmary. The appointment is for 4 notional half-days a week. Candidates must possess a registrable qualification and either F.R.C.S. (England, Edinburgh or Ireland) and the D.L.O. or F.R.C.S. in Otology.

Applications (1 copy only), giving full particulars of age, qualifications, &c., and details of present and previous appointments, together with the names of 3 persons to whom reference may be made, should reach the Secretary, The United Liverpool Hospitals, 80, Rodney-street, Liverpool, 1, by 26th July, 1958.

MANCHESTER REGIONAL HOSPITAL BOARD. Locum CONSULTANT OPHTHALMOLOGIST required for Wigan and Leigh Group of hospitals for 1 month from 1st August, and possibly longer. 7 half-days weekly. Salary according to personal grading.

Applications, giving details of experience and the names of 2 referees, to be sent to the Secretary, Wigan and Leigh Hospital Management Committee, Knowsley House, Wigan, as soon as possible.

MANCHESTER REGIONAL HOSPITAL BOARD. Part-time (8 half-days weekly) additional CONSULTANT GENERAL SURGEON to the Bury and Rossendale Group of hospitals (mainly at Bury General Hospital, 186 Beds). Wide experience and higher qualifications essential; appointee to live in area.

Application forms from the Senior Administrative Medical Officer to the Board, Cheetwood-road, Manchester, 8, to be returned by 28th July, 1958.

MANCHESTER REGIONAL HOSPITAL BOARD. Whole-time RESIDENT ASSISTANT PSYCHIATRIST (Senior Hospital Medical Officer), Whittingham (Mental) Hospital, near Preston (about 3200 Beds). All modern forms of treatment are undertaken. D.P.M. desirable.

Application forms from the Senior Administrative Medical Officer to the Board, Cheetwood-road, Manchester, 8, to be returned by 21st July, 1958.

NEWCASTLE REGIONAL HOSPITAL BOARD. Assistant PATHOLOGIST (Senior Hospital Medical Officer), whole-time or maximum part-time, for the North West Durham Group of hospitals. The Group Pathology Laboratory is situated in the main hospital at Shotley Bridge (533 Beds), which is the regional thoracic surgery centre and has radiotherapy and plastic surgery units. Special experience in hæmatology and/or biochemistry is desirable.

Applications, with names and addresses of 3 referees, to Senior Administrative Medical Officer, Regional Hospital Board, Benfield-road, Newcastle upon Tyne, 6, within 28 days.

SCOTLAND. WESTERN REGIONAL HOSPITAL BOARD. Applications are invited for the following appointments:

ASSISTANT OPHTHALMOLOGIST at the Glasgow Eye Infirmary. The appointment will be whole-time or on the maximum part-time basis of 9 notional half-days per week. Salary (at age 32 and over) on the scale £1653 15s.–£52 10s.–£2126 5s.

Whole-time ASSISTANT PSYCHIATRIST at Ailsa Hospital, Ayr (formerly Glengall). The Hospital has a high admission-rate and active outpatient clinics. Modern semi-detached house available. Salary (at age 32 and over) on the scale £1653 15s.–£52 10s.–£2126 5s.

Applications (16 copies), stating date of birth, qualifications, experience, present appointment, and the names of 3 referees, to reach the Secretary, Western Regional Hospital Board, 64, West Regent-street, Glasgow, C.2, not later than 30 days after the publication of this advertisement.

OXFORD REGIONAL HOSPITAL BOARD invite applications for the post of ASSISTANT SENIOR MEDICAL OFFICER. The candidate appointed will be required to assist the Senior Administrative Medical Officer in the planning, organisation and staffing of the hospital and specialist services of the region, and to carry out such administrative and executive duties as may be assigned to him. Previous experience in medical administration essential and knowledge of mental health services desirable. Salary £1764–£84(4)–£1051(1)–£2205 p.a., subject to National Health Service (Superannuation) Regulations.

Applications, giving full details, together with the names and addresses of 3 referees, should reach the Secretary, 43, Banbury-road, Oxford, by 15th August, 1958. Further particulars on application.

SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time CONSULTANT PSYCHIATRIST required, to be designated Medical Superintendent of Kingsway Hospital, Derby. Modern house available.

Application form and further details from Senior Administrative Medical Officer, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield. Forms to be returned by 2nd August, 1958.

SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time CONSULTANT PSYCHIATRIST required to be designated Medical Superintendent of Balderton Hospital, near Newark, a new hospital with 252 Beds at present for all grades of mental defectives.

Application forms and further details from Senior Administrative Medical Officer, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield. Forms to be returned by 9th August, 1958.

SHEFFIELD. THE UNITED SHEFFIELD HOSPITALS. Applications invited for the appointment of Whole-time ASSISTANT CHEMICAL PATHOLOGIST (salary in accordance with Senior Hospital Medical Officer scale) in the above Teaching Hospitals. Experience of general pathology and of chemistry is essential; a higher qualification is desirable.

Applications, with the names of 3 referees, to be sent to the Chief Administrative Officer, The United Sheffield Hospitals, West-street, Sheffield, 1, not later than 19th July, 1958, from whom further details may be obtained.

SOUTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited for employment as a Whole-time Locum Tenens PSYCHIATRIST at the Crayford Child Guidance Clinic, Woodside-road, Bexleyheath, Kent. The engagement is expected to last for approximately 4–5 months, and is available immediately.

Applications, giving the usual particulars and the names and addresses of 2 referees, should be sent to the Senior Administrative Medical Officer, South East Metropolitan Regional Hospital Board, 11A, Portland-place, W.1, as soon as possible.

SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD requires a Locum Tenens RADIOLOGIST of Senior Registrar, Senior Hospital Medical Officer, or Consultant status, for 9 sessions weekly for the West Dorset Group of hospitals for 3 weeks commencing on 1st September, 1958. Applicants should have had considerable experience in radiology. Applicants may visit the hospitals concerned by arrangement with Mr. D. A. PINKHAM, S.H.A., Group Secretary, West Dorset Hospital Management Committee, Damers-road, Dorchester.

Applications (2 copies), stating age, qualifications and experience, and giving the names and addresses of 3 referees, to the Area Secretary, Highcroft, Romsey-road, Winchester, by 31st July, 1958.

NEW ZEALAND. THE OTAGO HOSPITAL BOARD, UNIVERSITY OF OTAGO. Assistant Director of Anæsthetic Services and Lecturer in Anæsthetics, Otago Medical School. Applications are invited for the position of ASSISTANT DIRECTOR OF ANÆSTHETIC SERVICES to The Otago Hospital Board and LECTURER in Anæsthetics, University of Otago, from persons holding a degree in Medicine at an approved University and who must either:—

(*a*) Hold a higher qualification in anæsthetics and have had 5 years' or more experience in this specialty; or

(*b*) Have been qualified for a period of 15 years or more and have had 8 years' or more practical experience in anæsthetics.

The salary payable is that under the Hospital Employment (Medical Officers) Regulations, viz: £2040–£2340 p.a. The commencing rate of salary within the scale will be dependent on the qualifications and experience of the appointee and will be determined by the Medical Officers Salaries Grading Committee.

The position is a full-time one and private practice is not permitted. The appointment is subject to termination by 3 months' notice in writing from either side.

Travelling expenses will be paid in accordance with the information contained in the Conditions of Appointment.

Conditions of appointment and application forms may be obtained from the Office of the High Commissioner for New Zealand, 415, The Strand, London, or from the undersigned.

Applications, stating age, qualifications and experience, together with health and chest certificates, and testimonials, will be received by the undersigned until 10 o'clock A.M. on Monday, 29th September, 1958.

W. A. WILLIAMSON, Secretary, Otago Hospital Board.

P.O. Box 946, Dunedin, N.Z.

WELSH REGIONAL HOSPITAL BOARD. Whole-time Locum Tenens CONSULTANT in General Medicine required Newport and East Monmouthshire Area immediately for approximately 3 months.

Applications, naming 2 referees, to Senior Administrative Medical Officer, Temple of Peace, Cathays Park, Cardiff.

WELSH REGIONAL HOSPITAL BOARD. Whole-time Locum Tenens CONSULTANT in Obstetrics and Gynæcology required Caernarvon and Anglesey area approximately 2 months from 27th July, 1958.

Applications, naming 2 referees, to Senior Administrative Medical Officer, Temple of Peace, Cathays Park, Cardiff.

WELSH REGIONAL HOSPITAL BOARD. Whole-time Locum Tenens ASSISTANT PSYCHIATRIST required Morgannwg Hospital, Bridgend, immediately for approximately 3 months.

Applications, naming 2 referees, to Senior Administrative Medical Officer, Temple of Peace, Cathays Park, Cardiff.

WELSH REGIONAL HOSPITAL BOARD. Whole-time Locum Tenens ASSISTANT TRAUMATIC SURGEON required Neath General Hospital 21st July–9th August, 1958.

Applications, naming 2 referees, to Senior Administrative Medical Officer, Temple of Peace, Cathays Park, Cardiff.

WELSH REGIONAL HOSPITAL BOARD. Whole-time Locum Tenens CONSULTANT in General Surgery required Merthyr and Aberdare Area 4th–31st August, 1958.

Applications, naming 2 referees, to Senior Administrative Medical Officer, Temple of Peace, Cathays Park, Cardiff.

IBADAN, NIGERIA. UNIVERSITY COLLEGE HOSPITAL. General Outpatient Department. SENIOR HOSPITAL MEDICAL OFFICER. 3 SENIOR HOUSE OFFICERS/REGISTRARS. Applications are invited from registered medical practitioners for the above appointments in the General Outpatient Department of the new Teaching Hospital. The General Outpatient Clinic selects cases for the Consultant clinics, and with 3000 new patients a month provides clinical work of great variety and interest in both general and tropical medicine in adults and children.

Applicants for the post of Senior Hospital Medical Officer should have had wide clinical experience, including paediatrics, will be required to serve also in the Staff Medical Service, and must be capable of administering the combined departments in the absence of the Senior Hospital Medical Officer In Charge. The successful candidate will be offered an initial appointment of 2 tours of 12–18 months, renewable by mutual consent for a further tour.

The successful candidates for Senior House Officer/Registrar posts will be offered a contract for 1 tour of 12 months in the appropriate grade.

The salaries offered for the posts are:—

Senior Hospital Medical Officer: £1482 rising by 8 annual increments to a maximum of £1986, plus an inducement allowance payable to an expatriate doctor of £300 p.a. Point of entry into the salary scale will be determined by the qualifications and experience of the successful candidate.

Registrar: £1164 p.a., plus an inducement allowance payable to an expatriate doctor of £270 p.a.

Senior House Officer: £1116 p.a., plus an inducement allowance payable to an expatriate doctor of £270 p.a.

On satisfactory completion of the agreement a gratuity of £37 10s. will be paid for each completed period of 3 months' service.

An outfit allowance of £60 is payable on first appointment.

Partly-furnished quarters are provided at a rental of 8½% of salary, excluding inducement allowance, and an expatriate doctor appointed will be eligible for 7 days' leave on full pay for each completed month of service in Nigeria. A Nigerian doctor qualifies for 5 days' leave for each completed month of service.

Free first class passages are provided for expatriate doctors and their wives on first appointment, vacation leave and on completion of the agreement. Free first-class passages to Nigeria will, in certain circumstances, be provided for non-expatriate doctors.

Candidates will be eligible for children's allowances in accordance with existing regulations.

Arrangements can be made to enable doctors to continue their National Health Service Superannuation Scheme contributions, and details of the revised salary and gratuity payable in such cases will accompany application forms.

Applications should be submitted not later than 25th July, 1958, on the appropriate forms, which will be forwarded, together with additional information, on receipt of an addressed foolscap envelope by the Adviser on Staff Recruitment, London Office (University College Hospital, Ibadan), 57, Catherine-place, Palace-street, S.W.1.

Hospital Services: Junior Appointments

BETHNAL GREEN HOSPITAL, Cambridge Heath-road, London, E.2. HOUSE SURGEON, pre-registration post vacant 21st July.

Applications, stating experience, and copies of 2 testimonials, to Hospital Secretary.

BETHNAL GREEN HOSPITAL, Cambridge Heath-road, London, E.2. HOUSE SURGEON, gynæcology and obstetrics, pre-registration post, vacancy 24th July.

Applications, stating experience and copies of 2 testimonials, to Hospital Secretary.

BOLINGBROKE HOSPITAL, Wandsworth Common, S.W.11. Locum SURGICAL REGISTRAR, resident, 4th August–1st September, 1958, inclusive. F.R.C.S. essential.

Apply Hospital Secretary.

CENTRAL MIDDLESEX HOSPITAL, Park Royal, N.W.10. RESIDENT HOUSE OFFICER (pre-registration) required in General Medical Department including hæmatology and endocrinology. Post vacant 1st August, 1958.

Applications, with 2 testimonials, to Medical Director by 19th July.

CENTRAL MIDDLESEX HOSPITAL, Park Royal, N.W.10. RESIDENT HOUSE OFFICER (pre-registration) required in General Surgical and Urological Department. Post vacant 1st August, 1958.

Applications, with 2 testimonials, to Medical Director by 19th July.

CENTRAL MIDDLESEX HOSPITAL, Park Royal, London, N.W.10. RESIDENT SENIOR HOUSE OFFICER required for Casualty Department. Successful candidate will work under supervision of Orthopædic and Traumatic Specialist. Appointment for 6 months from 25th August.

Applications, with names of 2 referees or copies of testimonials, to Medical Director by 19th July.

CENTRAL MIDDLESEX HOSPITAL, Park Royal, London, N.W.10. RESIDENT HOUSE OFFICER required in Orthopædic and Traumatic Department. Post vacant 25th August.

Applications, with 2 testimonials, to Medical Director by 19th July.

CENTRAL MIDDLESEX HOSPITAL, Park Royal, N.W.10. RESIDENT HOUSE OFFICER (pre-registration) required in Surgical Department. Post vacant 1st August, 1958.

Applications, with 2 testimonials, to Medical Director by 19th July.

ELIZABETH GARRETT ANDERSON HOSPITAL, Euston-road, N.W.1. (ROYAL FREE HOSPITAL GROUP.) Applications are invited from pre-registration and registered Women medical practitioners for the post of OBSTETRIC HOUSE SURGEON (recognised for the M.R.C.O.G.) Duties to commence 1st September, 1958. Appointment for 6 months. Salary in accordance with Ministry of Health scale for House Officer.

Applications, with copies of 3 recent testimonials, to be sent to the Secretary, Elizabeth Garrett Anderson Hospital, by 23rd July, 1958.

ELIZABETH GARRETT ANDERSON HOSPITAL, Euston-road, N.W.1. Applications are invited from pre-registration and registered Women medical practitioners for the post of FIRST HOUSE SURGEON with charge of general surgical beds. 6-month appointment, to start as soon as possible. Salary according to Ministry of Health scale for House Officers.

Applications, with copies of 3 recent testimonials, should be sent to the Secretary, Elizabeth Garrett Anderson Hospital, by 23rd July.

GERMAN HOSPITAL, London, E.8. (General—157 Beds.) Applications for the 6-month resident appointment, vacant 1st August, of Registered HOUSE PHYSICIAN should be sent to Group Secretary, Hackney Hospital, E.9, by 21st July, quoting GH/HP.

GERMAN HOSPITAL, London, E.8. (General—157 Beds.) Applications for the resident appointment, from 1st August, of SENIOR HOUSE OFFICER (general surgery) (recognised for F.R.C.S.), should be sent to Group Secretary, Hackney Hospital, E.9, by 21st July, quoting GH/SHO.

GROUP LABORATORY, Mile End Hospital, Bancroft-road, London, E.1. RESIDENT ASSISTANT PATHOLOGIST (Senior House Officer grade). Previous experience an advantage but not essential. Laboratory recognised for Diploma of Pathology and is well equipped with excellent training facilities. Post vacant 28th July, 1958.

Applications, stating age, nationality, qualifications, experience, and copies of not more than 3 testimonials, to the Secretary, Stepney Group Hospital Management Committee, Mile End Hospital, Bancroft-road, London, E.1.

HACKNEY HOSPITAL, London, E.9. (General—857 Beds.) Applications for the 6-month resident appointment, now vacant, of Registered HOUSE SURGEON (obstetrics and gynæcology), should reach Secretary, above address, by 21st July, quoting HH/HSO.

HAMMERSMITH HOSPITAL AND POSTGRADUATE MEDICAL SCHOOL, Ducane-road, London, W.12. Whole-time NON-RESIDENT REGISTRAR (general surgery) required. Experience with extracorporeal circulation methods would be an advantage.

Detailed applications, names 2 referees, to Secretary, Board of Governors, The Hammersmith, West London and St. Mark's Hospitals, Ducane-road, London, W.12, by 21st July.

LAMBETH HOSPITAL, Brook-drive, S.E.11. Applications are invited from pre-registration and registered medical practitioners for the appointment of RESIDENT HOUSE SURGEON in the Obstetric and Gynæcological Unit. Appointment is for 6 months from 1st September, 1958. It would be convenient if the successful candidate could carry out a fortnight's locum duty, commencing 18th August, 1958. Hospital recognised for M.R.C.O.G. and D.Obst.R.C.O.G.

Application forms from the Secretary. Self-addressed envelope should be enclosed.

LAMBETH HOSPITAL, Kennington, S.E.11. Applications are invited from pre-registration and registered medical practitioners for the post of RESIDENT HOUSE SURGEON. Recognised for the F.R.C.S. Vacant 24th August, 1958. The successful candidate will be required to carry out a fortnight's locum duty commencing 10th August.

Application forms from the Hospital Secretary.

LONDON HOSPITAL, Whitechapel, E.1. Applications are invited for the post of SENIOR REGISTRAR to the Department of Thoracic Surgery. Candidates must be Fellows of one of the Royal Colleges of Surgeons.

Applications (12 copies), giving the names and addresses of 3 referees, should reach the undersigned by Monday, 28th July, 1958. H. BRIERLEY, House Governor.

NELSON HOSPITAL, Kingston-road, Merton, S.W.20. HOUSE SURGEON (resident, not pre-registration). Post vacant now. Recognised for F.R.C.S.

Applications, stating age, qualifications, &c., with the names and addresses of 2 referees, should be sent to the Secretary at above address.

MILDMAY MISSION HOSPITAL, Austin-street, London, E.2. Applications are invited for the pre-registration post of RESIDENT HOUSE SURGEON (post recognised for F.R.C.S.) vacant on 31st July, 1958. Candidates should be in sympathy with the evangelical Christian aims of the Hospital.

Applications and references to be addressed to the Medical Superintendent as soon as possible.

MILDMAY MISSION HOSPITAL, Austin-street, London, E.2. Applications are invited for the pre-registration post of RESIDENT HOUSE PHYSICIAN/CASUALTY OFFICER, vacant on 31st July, 1958. Candidates should be in sympathy with the evangelical Christian aims of the Hospital.

Applications and references to be addressed to the Medical Superintendent as soon as possible.

MEMORIAL HOSPITAL, Shooters-hill, Woolwich, S.E.18. SENIOR HOUSE OFFICER (Casualty Department). Vacant 8th August. Recognised for F.R.C.S. 6 months' resident appointment and may then be renewed. Salary £819 10s. p.a., less £150 p.a. for residence.

Apply to Group Secretary, Memorial Hospital, Woolwich, S.E.18.

MILE END HOSPITAL, Bancroft-road, London, E.1. (479 Beds.) HOUSE SURGEON (obstetrics and gynæcology) (post-registration). Recognised for D.Obst.R.C.O.G. Post vacant 4th August, 1958.

Application forms, obtainable from Physician-Superintendent, to be returned by 25th July, 1958, with copies of not more than 3 testimonials.

ROYAL EYE HOSPITAL, St. George's Circus, S.E.1. Locum CASUALTY OFFICER (Senior House Officer grade) required, mid-July–1st October. Successful candidate will be eligible to apply for this and other house appointments vacant on 1st October.

Applications to the Secretary.

ROYAL FREE HOSPITAL, Gray's Inn-road, W.C.1. Applications are invited for the post of RESIDENT SENIOR HOUSE OFFICER to the Radiotherapy Department. Applicants should be registered medical practitioners, and the appointment is suitable for a candidate doing a postgraduate course in radiotherapy. The appointment is for 1 year in the first instance. Duties to commence 1st October, 1958.

Application forms may be obtained from the Secretary to the Board of Governors, Royal Free Hospital, Gray's Inn-road, W.C.1, to whom they should be returned not later than 25th July, 1958.

ROYAL FREE HOSPITAL, Gray's Inn-road, W.C.1. Applications are invited for the post of Part-time REGISTRAR (4 sessions) in the Dermatological Department, to commence on 1st October, 1958, which will be tenable for 1 year in the first instance. The post is at present held by a Locum Tenens who will be an applicant for the appointment.

Application forms may be obtained from the Secretary to the Board of Governors, to whom they should be returned not later than 25th July, 1958.

ROYAL FREE HOSPITAL, Gray's Inn-road, London, W.C.1. Applications are invited from registered medical practitioners for 2 whole-time, non-resident posts of REGISTRAR in Clinical Pathology. Both appointments for 1 year in the first instance from 1st October, 1958. Experience in clinical pathology essential.

Application forms, which may be obtained from the Secretary to the Board of Governors at the above address, should be returned not later than 26th July, 1958.

ROYAL FREE HOSPITAL, W.C.1. Applications are invited for the post of MEDICAL REGISTRAR (non-resident) at the Lawn-road Branch of the Royal Free Hospital. Duties to commence on 1st October, 1958. Appointment for 1 year in the first instance. Candidates should be registered medical practitioners and members of the Royal College of Physicians.

Application forms may be obtained from the Secretary to the Board of Governors, to whom they should be returned not later than 1st August, 1958.

ROYAL FREE HOSPITAL. Applications are invited from registered medical practitioners for the post of REGISTRAR (non-resident) to the E.N.T. Department of the Royal Free Hospital. Duties to commence on 1st October, 1958.

Application forms may be obtained from the Secretary to the Board of Governors, The Royal Free Hospital, Gray's Inn-road, W.C.1, to whom they should be returned not later than 1st August, 1958.

ROYAL NORTHERN HOSPITAL, Holloway, N.7. Applications are invited for the post of SENIOR HOUSE OFFICER (orthopædics), vacant 28th July, 1958. Occasional casualty duties. Recognised for F.R.C.S.

Applications, with copies of recent testimonials, to be sent to the Hospital Secretary by 19th July, 1958.

SOUTH EAST REGIONAL THORACIC SURGERY UNIT (50 Beds), BROOK GENERAL HOSPITAL, Shooters Hill-road, S.E.18. SENIOR HOUSE OFFICER. Vacant mid-August. Recognised for F.R.C.S. 6 months' appointment and may then be renewed for a further period. The Unit treats all types of chest diseases and offers opportunity for comprehensive training in thoracic surgery.

Apply to Group Secretary, Memorial Hospital, Woolwich, S.E.18.

SOUTH LONDON HOSPITAL FOR WOMEN AND CHILDREN, Clapham Common, S.W.4. SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited from registered Women medical practitioners for the post of ANÆSTHETIC REGISTRAR (either resident or prepared to live within 20 minutes of the Hospital). D.A. desirable but not essential. Post recognised for D.A. and F.F.A. R.C.S. The appointment is normally for 2 years but subject to review at the end of 1 year. Vacant now. Canvassing will disqualify, but candidates may visit the Hospital by arrangement.

Forms of application from the Group Secretary, Lambeth Group Hospital Management Committee, Renfrew-road, S.E.11, to be returned by 26th July.

SOUTH LONDON HOSPITAL FOR WOMEN AND CHILDREN, Clapham Common, S.W.4. Applications are invited for pre-registration and registered Female medical practitioners for the appointment of GYNÆCOLOGICAL HOUSE SURGEON Vacant 10th September, 1958. Recognised for the M.R.C.O.G.

Application forms from the Secretary.

ST. NICHOLAS HOSPITAL, Plumstead, S.E.18. Senior HOUSE OFFICER (Casualty, Orthopædic and Fracture Departments). Vacant early August. Recognised for F.R.C.S. 6 months' resident appointment and may then be renewed. Salary £819 10s. p.a. less £150 p.a. for residence.

Apply to Group Secretary, Memorial Hospital, Woolwich, S.E.18.

ST. ANDREW'S HOSPITAL, Devons-road, Bow, E.3. SENIOR HOUSE OFFICER in Pathology required at above Hospital. No previous experience necessary. Training in all branches of pathology available. Post vacant 1st August, 1958.

Apply to Group Secretary, Bow Group Hospital Management Committee, 2A, Bow-road, E.3.

ST. ANDREW'S HOSPITAL, Bow, E.3. House Physician required. Recognised pre-registration post.

Applications, with copy of at least 1 testimonial, to the Hospital Secretary.

ST. ANDREW'S HOSPITAL, Devons-road, Bow, E.3. HOUSE SURGEONS (2). Recognised pre-registration appointments.

Applications, with copy of at least 1 testimonial, should be sent to Hospital Secretary immediately.

ST. CHARLES' HOSPITAL, Ladbroke-grove, W.10. Applications are invited for the post of SENIOR HOUSE OFFICER (pædiatrics, geriatrics and general wards).

Applications, stating age, qualifications and experience, together with names of 2 referees, to Hospital Secretary immediately.

ST. CLEMENT'S HOSPITAL, Bow, E.3. House Physician (not pre-registration) for general medical wards. Post vacant 18th July, 1958.

Applications, stating age, qualifications and experience, together with the names and addresses of 2 referees, to be sent to Hospital Secretary immediately.

ST. JAMES' HOSPITAL, Balham, London, S.W.12. HOUSE SURGEON (genitourinary and general surgery). Post vacant 17th September.

Applications, stating age, qualifications, experience, and the names and addresses of 2 referees, to Group Secretary, Wandsworth Hospital Group, at above address by 26th July.

ST. JAMES' HOSPITAL, Balham, London, S.W.12. Locum REGISTRAR (orthopædic and trauma) required from 21st to 30th July inclusive (resident).

Applications, giving full particulars and names of 2 referees, to Group Secretary, Wandsworth Hospital Group, at above address immediately.

ST. LEONARD'S HOSPITAL, Nuttall-street, N.1. (Acute General—192 Beds.) Applications are invited for the post of SENIOR HOUSE OFFICER in General Medicine. The appointment is for 12 months and is vacant on 26th August, 1958.

Applications, with 2 testimonials, to the Hospital Secretary by 25th July, 1958.

ST. MARY'S HOSPITAL, W.2. Casualty Surgeon, graded Senior House Officer (non-resident), for a first period from a date to be arranged in August, until 28th February, 1959.

Applications, giving full details, with names and addresses of 3 referees, should reach the House Governor not later than 28th July, 1958.

ST. PETER'S, ST. PAUL'S AND ST. PHILIP'S HOSPITALS. RESIDENT SURGICAL OFFICER (Senior Registrar grade) required for St. Peter's Hospital on 1st October, 1958. Applications invited from Male candidates on the British Register who have completed their training in general surgery. Appointment for 6 months, with opportunity for a further 6 months if recommended. Candidate should be prepared to spend 1 year at the Hospital if required.

Applications (12 copies) and the names of 3 referees, should reach the House Governor, St. Peter's Hospital, Henrietta-street, W.C.2, by 19th July, 1958.

ST. STEPHEN'S HOSPITAL, Chelsea, S.W.10. Pædiatric HOUSE PHYSICIAN (with some dermatology duties). Resident. Vacancy late July.

Applications, naming 2 referees, to Medical Superintendent within 7 days.

ST. STEPHEN'S HOSPITAL, Chelsea, S.W.10. Obstetric AND GYNÆCOLOGICAL HOUSE SURGEON. Resident. Post-registration. Post recognised for D.Obst.R.C.O.G. Vacancy mid-August.

Applications, naming 2 referees, to Medical Superintendent within 14 days of date of advertisement.

ST. THOMAS'S HOSPITAL, London, S.E.1. Resident REGISTRAR to the Department of Obstetrics and Gynæcology. For a period of 1 year in the first instance.

Applications, naming 2 referees, to the Clerk to the Governors by 21st July, 1958.

THE HOSPITAL FOR SICK CHILDREN, Great Ormond-street, London, W.C.1. There will be a vacancy on 6th September, 1958, for an ASSISTANT RESIDENT MEDICAL OFFICER (Senior House Officer) at the country branch hospital, Tadworth, Surrey (101 Beds).

Further particulars and form of application, which must be returned by 28th July, 1958, are obtainable from the undersigned.

H. F. RUTHERFORD, House Governor and Secretary.

WANSTEAD HOSPITAL, Harmon-hill, London, E.11. (191 Beds.) HOUSE SURGEON required. Post vacant 28th July, 1958. Recognised for F.R.C.S.

Applications, with full details and copies of 2 recent testimonials, should be sent immediately to Secretary, Forest Group Hospital Management Committee, Langthorne-road, E.11.

WANSTEAD HOSPITAL, Harmon-hill, E.11. (191 Beds.) Applications invited for post of SENIOR (RESIDENT) HOUSE OFFICER, vacant 26th July. Salary £819 10s. p.a. less £150 p.a. for board-residence. Post includes care of general surgical and orthopædic cases and duties in casualty department. Post recognised for F.R.C.S. examination.

Applications, stating age, qualifications, experience, together with copies of 2 recent testimonials, should be sent to Secretary, Forest Group Hospital Management Committee, Langthorne-road, E.11.

WILLESDEN GENERAL HOSPITAL, Harlesden-road, N.W.10. Locum RESIDENT CASUALTY OFFICER required 7th–31st August. £15 19s. p.w.

Apply Hospital Secretary.

WHIPPS CROSS HOSPITAL, Leytonstone, E.11. LEYTONSTONE (NO. 10) HOSPITAL GROUP. Applications are invited for the post of Pre-registration HOUSE PHYSICIAN (general medicine) which becomes vacant 1st September, 1958.

Application forms are obtainable from the Hospital Secretary, to whom they should be returned by 22nd July, 1958.

ABERYSTWYTH, CARDIGANSHIRE. GENERAL HOSPITAL. MID-WALES HOSPITAL MANAGEMENT COMMITTEE. HOUSE OFFICER (surgical) required (resident). Post recognised for F.R.C.S. examination. Vacancy immediate.

Applications, stating age, experience, &c., to the Group Secretary, Mid-Wales Hospital Management Committee, 31, North-parade, Aberystwyth, Cardiganshire.

ALTON, HAMPSHIRE. HENRY GAUVAIN HOSPITAL. (112 Beds.) ALTON GROUP HOSPITAL MANAGEMENT COMMITTEE. SENIOR HOUSE OFFICER required for the above Hospital for a period in the first instance of 6 months. Post vacant 1st August, 1958. Non-pulmonary tuberculosis, orthopædic and general surgery. Primary or Final F.R.C.S. candidate preferred, married or single, to live in small cottage on estate.

Applications, together with the names and addresses of 3 referees, to Hospital Secretary, Henry Gauvain Hospital, Alton, Hants.

ASHFORD HOSPITAL, Ashford, Middlesex. (560 Beds.) STAINES GROUP HOSPITAL MANAGEMENT COMMITTEE. Required, RESIDENT SENIOR HOUSE OFFICER for General Medical duties.

Applications, stating age, qualifications and experience, with copies of up to 3 recent testimonials, to Medical Director of Hospital immediately.

AYLESBURY, BUCKINGHAMSHIRE. ROYAL BUCKINGHAMSHIRE HOSPITAL. Accident and orthopædic and children's general surgery. SENIOR HOUSE OFFICER required 1st August. Recognised for F.R.C.S.

Apply, with 2 names for reference, to Secretary-Superintendent.

BARNSTAPLE, NORTH DEVON INFIRMARY. (105 Beds.) HOUSE SURGEON (pre-registration) required from mid-July.

Applications, naming 2 referees, to Group Secretary, 19, Alexandra-road, Barnstaple, N. Devon.

BECKENHAM HOSPITAL, Kent. (100 Beds.) House SURGEON required at above Hospital immediately. Recognised for F.R.C.S. Pre-registration post, with continuity for further 6 months in House Physician post, subject to satisfactory service.

Apply, stating age, qualifications and experience, and naming 3 referees, to Administrative Officer.

BEDFORD GENERAL HOSPITAL. (431 Beds.) House SURGEON required. Pre- or post-registration ; recognised for F.R.C.S. Vacant early July. Post offers exceptional opportunities for general experience in busy acute surgical units.

Enquiries and applications, with copies of 2 recent testimonials, to be sent immediately to Group Secretary, Bedford Group Hospital Management Committee, 3, Kimbolton-road, Bedford.

BEDFORD GENERAL HOSPITAL. (431 Beds.) Resident Pre-registration HOUSE PHYSICIAN, post vacant 25th July.

Applications, stating age, qualifications, experience, and copies of 2 recent testimonials, to Group Secretary, Bedford Group Hospital Management Committee, 3, Kimbolton-road, Bedford.

BEVERLEY, YORKSHIRE. WESTWOOD HOSPITAL. (229 Beds.) HOUSE SURGEON (House Officer or Senior House Officer grade according to experience). Vacant now. General surgical duties, some orthopædics. Offers good opportunity for general experience in busy acute general hospital. Recognised for F.R.C.S. Approved pre-registration post but fully registered practitioners may apply.

Applications to Group Secretary, Westwood Hospital, Beverley, Yorkshire.

BEVERLEY, YORKSHIRE. WESTWOOD HOSPITAL. (229 Beds.) HOUSE PHYSICIAN. Vacant 1st August. Pre-registration post, but fully registered practitioners may apply. Married quarters may be available.

Detailed applications to Group Secretary, Westwood Hospital, Beverley, Yorkshire.

BEXHILL HOSPITAL, Bexhill-on-Sea. (61 Beds.) House SURGEON (resident) required. Pre-registration post vacant now. National scale of salary.

Apply to Hospital Administrator.

BEXHILL HOSPITAL, Bexhill-on-Sea. (61 Beds.) Senior HOUSE OFFICER. Applications are invited for this post (resident preferred) for a period of 1 year. National scale of salary.

Apply to Hospital Administrator.

BIRMINGHAM, 18. DUDLEY ROAD HOSPITAL. Senior HOUSE OFFICER in Anæsthetics (resident). Vacant 1st August, 1958. Recognised for D.A. and F.F.A. R.C.S. Extensive experience not necessary. Duties include list and emergency work in general surgery, gynæcology, obstetrics and E.N.T. at hospitals within the Group.

Detailed applications, with names of 2 referees, to Group Secretary.

BIRMINGHAM, 29. SELLY OAK HOSPITAL. (Equipped beds—1033.) HOUSE SURGEONS (pre-registration), 2 now vacant, 1 vacant 1st August. Recognised for F.R.C.S.

Apply immediately to the Medical Superintendent, giving qualifications, age, experience and enclosing copies of 3 testimonials.

BIRMINGHAM. SOLIHULL HOSPITAL, Lode-lane, SOLIHULL. HOUSE PHYSICIAN (pre-registration). Now vacant. General hospital offering good experience. 5 other resident medical staff.

Applications, with names of 2 referees, to Medical Superintendent immediately.

BIRMINGHAM. SOLIHULL HOSPITAL, Lode-lane, SOLIHULL. HOUSE SURGEON (pre-registration). General hospital offering good experience. 5 other resident medical staff.

Applications, with names of 2 referees, to Medical Superintendent immediately.

BIRMINGHAM. SOLIHULL HOSPITAL, Lode-lane, SOLIHULL. OBSTETRIC HOUSE SURGEON (pre-registration). Now vacant.

Applications, stating age, qualifications and names of referees, to Medical Superintendent immediately.

BIRMINGHAM REGIONAL HOSPITAL BOARD.

(1) **Coventry Group, Coventry and Warwickshire Hospital, Coventry**

(*a*) REGISTRAR (anæsthetics), Coventry and Warwickshire Hospital, Coventry. Experience specialty essential. Recognised F.F.A. R.C.S. Resident.

(*b*) REGISTRAR (general medicine). Duties mainly at Coventry and Warwickshire Hospital, Coventry (354 Beds). Experience specialty essential. Higher qualifications desirable. Resident.

(2) **Birmingham Group, Hollymoor Hospital, Birmingham, 31**

REGISTRAR, resident non-resident. Hollymoor Hospital (750 Beds), Birmingham. Experience in investigation, diagnosis and treatment of all psychiatric illness. D.P.M. course, Birmingham University.

(3) **Birmingham (Dudley Road) Group, Dudley Road Hospital, Birmingham, 18**

REGISTRAR (surgical), resident, required. St. Chad's Hospital, Birmingham, 16. (50 general surgical beds.) Recognised for F.R.C.S. Limited married accommodation available.

(4) **Walsall Group, Walsall General (Sister Dora) Hospital, Walsall**

REGISTRAR (general surgery). Experience specialty essential. Manor Hospital, Walsall. (333 Beds.) Married quarters available.

Application forms from Group Secretaries, to be returned by 21st July, 1958.

BIRMINGHAM (SANATORIA) GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of JUNIOR HOSPITAL MEDICAL OFFICER at West Heath Hospital, Rednal-road, Birmingham, 31 (207 Beds for the treatment of tuberculous and non-tuberculous chest cases). The successful applicant will reside at the above Hospital (accommodation for single person only), and will be offered facilities for undertaking duties at the Birmingham Chest Clinic, Great Charles-street, Birmingham, 3.

Applications, stating age, qualifications, training and experience, together with copies of 3 recent testimonials, should be addressed to the Group Secretary, Birmingham (Sanatoria) Group Hospital Management Committee, Yardley Green Hospital, Birmingham, 9.

BIRMINGHAM. THE UNITED BIRMINGHAM HOSPITALS. THE CHILDREN'S HOSPITAL, Ladywood-road, BIRMINGHAM, 16. Applications are invited for the post of RESIDENT SURGICAL OFFICER (Registrar), vacant 7th September, 1958, for 1 year. Preference will be given to applicants with a higher qualification. Post offers wide practical experience and contact with all specialist departments including thoracic unit.

Forms of application and further details of the post may be obtained from the House Governor and should be returned by 26th July, 1958. G. A. PHALP, Secretary to the Board of Governors.

BIRMINGHAM. THE UNITED BIRMINGHAM HOSPITALS. Applications are invited for the post of RESIDENT ANÆSTHETIST (Senior House Officer grade) for duties in the United Hospitals and resident at the General Hospital or at the Queen Elizabeth Hospital. The post is tenable for 1 year. The appointment is recognised for the purpose of taking the F.F.A. R.C.S. examination.

Application forms may be obtained from the Secretary, United Birmingham Hospitals, Queen Elizabeth Hospital, Edgbaston, Birmingham, 15, and should be returned to him as soon as possible.

BIRMINGHAM. THE UNITED BIRMINGHAM HOSPITALS. Applications are invited for the post of REGISTRAR in Radiotherapy (non-resident Registrar grade) for duties in the Radiotherapy Departments of the United Birmingham Hospitals. Candidates should, if possible, hold additional qualifications in medicine, surgery, gynæcology, or physics, or a Diploma in Radiotherapy.

Application forms may be obtained from the Secretary, United Birmingham Hospitals, Queen Elizabeth Hospital, Edgbaston, Birmingham, 15, and should be returned by 26th July, 1958.

BIRMINGHAM. THE UNITED BIRMINGHAM HOSPITALS. Applications are invited for the appointment of SURGICAL REGISTRAR (Registrar grade) to the United Birmingham Hospitals. Candidates should hold at least a primary Fellowship qualification, and may be required to be resident.

Forms of application from the Secretary, United Birmingham Hospitals, Queen Elizabeth Hospital, Edgbaston, Birmingham, 15, to be returned by 26th July, 1958.

BIRMINGHAM. THE UNITED BIRMINGHAM HOSPITALS. Applications are invited for the appointment of SURGICAL REGISTRAR (Registrar grade) to the United Birmingham Hospitals, for duty in the Casualty Department at the General Hospital. Candidates should hold at least a Primary Fellowship qualification. The successful candidate will be required to be resident on rota. A scheme for the interchange, at the level of Registrar, between the Casualty Department of the General Hospital and 1 of the Registrar appointments at the Royal Orthopædic Hospital has been agreed between the United Birmingham Hospitals and the Birmingham Regional Hospital Board, and the successful candidate may be required to spend not more than a year in such interchange.

Forms of application from the Secretary, United Birmingham Hospitals, Queen Elizabeth Hospital, Edgbaston, Birmingham, 15, to be returned by 26th July, 1958.

BIRMINGHAM, 9. LITTLE BROMWICH GENERAL HOSPITAL. HOUSE SURGEON (Male Female). Now vacant. Recognised as pre-registration appointment.

Apply Physician-Superintendent, with copies of 2 testimonials or names of referees.

BIRMINGHAM, 9. LITTLE BROMWICH GENERAL HOSPITAL. HOUSE PHYSICIAN (Male-Female). Now vacant. Recognised pre-registration appointment.

Apply Physician-Superintendent, with copies of 2 testimonials or names of referees.

BIRMINGHAM, 9. LITTLE BROMWICH GENERAL HOSPITAL. RESIDENT MEDICAL OFFICER in Infectious Diseases (Senior House Officer grade). Hospital serves a wide area and gives opportunities for the study of infectious diseases, and has a poliomyelitis respiratory unit. Part of the Hospital is being developed as a General Hospital, where further experience can be gained.

Apply Physician-Superintendent, with 2 testimonials.

BISHOP AUCKLAND. THE GENERAL HOSPITAL. SOUTH WEST DURHAM HOSPITAL MANAGEMENT COMMITTEE. Applications invited from registered or pre-registration practitioners for post of HOUSE OFFICER (obstetrics and gynæcology) vacant 1st September, 1958. Recognised for D.Obst. R.C.O.G. Departmental beds 69.

Apply, naming 2 referees, to Group Secretary at above address.

BISHOP AUCKLAND. THE GENERAL HOSPITAL. (350 Beds.) SOUTH WEST DURHAM HOSPITAL MANAGEMENT COMMITTEE. HOUSE SURGEON required. Recognised pre-registration appointment. Accommodation available for married officer with no children.

Apply, naming 2 referees, to Group Secretary by 19th July.

BISHOP'S STORTFORD, HERTFORDSHIRE. HERTS AND ESSEX GENERAL HOSPITAL. Applications invited for post of HOUSE OFFICER (surgical—pre-registration). Salary £467 10s. -£522 10s. p.a. less £125 for residential emoluments. Appointment to commence immediately.

Applications, stating age, nationality, qualifications and experience, with copies of 2 testimonials or names of referees, to Hospital Secretary.

BLACKBURN AND DISTRICT HOSPITAL MANAGE- MENT COMMITTEE. ROYAL INFIRMARY AND QUEEN'S PARK HOSPITAL, BLACKBURN. SENIOR HOUSE OFFICER for E.N.T. Department (32 Beds); 2 Consultants in specialty. Recognised for D.L.O. and F.R.C.S.

Apply to Group Secretary, Hospital Management Committee Office, Royal Infirmary, Blackburn.

BLACKBURN AND DISTRICT HOSPITAL MANAGE- MENT COMMITTEE.

Royal Infirmary, Blackburn

HOUSE SURGEON required for 28th July, 1958. Post recognised for F.R.C.S. and approved for pre-registration purposes.

Queen's Park Hospital, Blackburn

HOUSE SURGEON required 23rd July, 1958. Recognised for F.R.C.S. and approved for pre-registration purposes.

Apply to Group Secretary, Hospital Management Committee Office, Royal Infirmary, Blackburn.

BLACKPOOL VICTORIA HOSPITAL. (354 Beds.) SENIOR HOUSE OFFICER (anæsthetics). Post recognised for F.F.A. R.C.S. and D.A. This is a busy general hospital offering a sound and varied experience in anæsthetics.

Applications, giving age, qualifications, experience, and the names and addresses of 2 referees, should be sent to the Hospital Secretary.

BLACKPOOL VICTORIA HOSPITAL. Senior House OFFICER (medical). This post offers varied experience for candidates interested in general medicine. Tenure of 1 year.

Applications, giving age, qualifications, experience, and the names and addresses of 2 referees, should be sent to the Hospital Secretary.

BOLTON. HULTON HOSPITAL. (131 Beds.) Resident MEDICAL OFFICER (Senior House Officer grade). Vacant 10th August and tenable for 12 months. Duties will be chiefly with 27 acute medical beds and 11 acute pædiatric beds, including infectious fevers. Duties will also include care of dermatological cases and some acute rheumatism and geriatric cases and may include outpatients and inpatients duties in other hospitals of the Group. Married quarters available.

Applications, stating age, nationality, qualifications and experience, to Group Secretary, Bolton and District Hospital Management Committee, The Royal Infirmary, Bolton.

BOLTON AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE.

Bolton District General Hospital (607 Beds)

RESIDENT HOUSE SURGEONS (2). Both now vacant, tenable for 6 months and recognised under pre-registration service scheme. Also recognised for F.R.C.S.

The Royal Infirmary, Bolton (238 Beds)

RESIDENT HOUSE SURGEONS (3). 1 vacant now, 1 15th July, and 1 1st August. Tenable for 6 months and recognised under pre-registration service scheme. Also recognised for F.R.C.S.

Applications, with the names of 2 referees, to Group Secretary, The Royal Infirmary, Bolton.

BOLTON DISTRICT GENERAL HOSPITAL. (607 Beds.) RESIDENT HOUSE PHYSICIAN. Vacant 1st August, tenable for 6 months and recognised under pre-registration service scheme.

Applications, with the names of 2 referees, to Group Secretary, Bolton and District Hospital Management Committee, The Royal Infirmary, Bolton.

BROMLEY HOSPITAL, Kent. Senior House Officer in charge of Casualty Department required end of August, for 6 months. Recognised for F.R.C.S.

Apply, stating age, qualifications with dates, previous experience, and naming 3 referees, to Administrative Officer.

BRIGHTON GENERAL HOSPITAL. Applications are invited for the appointment of HOUSE SURGEON to the Orthopædic Unit. Salary in accordance with national scales. This is a pre-registration appointment.

Applications, stating age, qualifications, and experience, and giving the names of 2 referees, should be sent to the Physician-Superintendent, Brighton General Hospital, Elm-grove, Brighton.

BRIGHTON GENERAL HOSPITAL. Applications are invited for the appointment of SENIOR HOUSE OFFICER (orthopædics). Recognised for F.R.C.S. examinations. Salary in accordance with national scale. Vacant 9th August, 1958.

Applications, stating age, qualifications, and experience, together with copies of recent testimonials, and giving the names of 2 referees, should be sent to the Physician-Superintendent, Brighton General Hospital, Elm-grove, Brighton, 7, as soon as possible.

BRIGHTON GENERAL HOSPITAL. Applications are invited for the appointment of HOUSE SURGEON (recognised for F.R.C.S.) to the General Surgical Unit (60 Beds). The post will be vacant on 1st August, 1958. Salary in accordance with national scale. Recognised as a pre-registration appointment.

Applications, stating age, qualifications, experience and giving the names of 2 referees, should be sent to the Physician-Superintendent, Brighton General Hospital, Elm-grove, Brighton, 7.

BRIGHTON AND LEWES HOSPITAL MANAGEMENT COMMITTEE GROUP HOSPITALS. (78 Beds.) SENIOR HOUSE OFFICER for duties in the E.N.T. Department of the above Group. Vacant beginning of August. Recognised for F.R.C.S. and D.L.O.

Applications, with details of experience, &c., together with names of 2 referees, to the Administrative Officer, Royal Sussex County Hospital, Brighton, 7.

BRIGHTON. ROYAL ALEXANDRA HOSPITAL FOR SICK CHILDREN, Dyke-road. (120 Beds and Cots.) BRIGHTON AND LEWES HOSPITAL MANAGEMENT COMMITTEE. Vacancy for SENIOR HOUSE OFFICER from 25th August, 1958. Salary at the rate of £819 10s. p.a., less £150 p.a. for residential emoluments. Candidates should have had experience in pædiatrics. The post is recognised for D.C.H.

Applications, stating age, nationality, experience, together with copies of 2 testimonials and the names of 2 referees, should reach the Administrative Officer not later than 24th July, 1958.

BRIGHTON. ROYAL SUSSEX COUNTY HOSPITAL. (314 Beds.) Locum SENIOR CASUALTY OFFICER (Junior Hospital Medical Officer) for 2 weeks commencing 24th July, 1958.

Applications, stating usual particulars, and naming 2 referees, to the Administrative Officer, Royal Sussex County Hospital, Brighton, 7.

BRIGHTON. SUSSEX EYE HOSPITAL. (58 Beds.) SENIOR HOUSE SURGEON (Senior House Officer grade) and HOUSE SURGEON required end of August. Both posts recognised for F.R.C.S. and D.O. Successful applicant for the post of House Surgeon will be considered for the senior post on completion of 6 months.

Applications, stating usual particulars, and naming 2 referees, to the Administrative Officer, Royal Sussex County Hospital, Brighton, 7.

BOURNEMOUTH AND EAST DORSET HOSPITAL MANAGEMENT COMMITTEE. BOURNEMOUTH CHILDREN'S UNIT. Applications are invited for the appointment of PÆDIATRIC SENIOR HOUSE OFFICER to the above Unit of 34 Beds which is situated at the Christchurch Hospital, Hants. Duties include the conduct of an Infant Welfare Centre. The post is recognised for the D.C.H. and becomes vacant on 10th September, 1958.

Applications, with copies of testimonials, to the Hospital Secretary, Christchurch Hospital, Hants, within 7 days of the appearance of this advertisement.

BRADFORD. ST. LUKE'S HOSPITAL. Locum Senior HOUSE OFFICER (general medicine and pathology). From 14th July to 24th August, inclusive.

Applications, stating age, nationality, qualifications and experience with copy testimonials, to Secretary, Royal Infirmary, Bradford.

BRISTOL. SOUTHMEAD GENERAL HOSPITAL GROUP MANAGEMENT COMMITTEE. Required at Southmead Hospital (570 Beds), RESIDENT SENIOR HOUSE OFFICER (casualty) with duties as Orthopædic House Surgeon for 6 or 12 months commencing 1st August, 1958. Post recognised for F.R.C.S. examination.

Applications to be submitted to the Group Secretary, Southmead Hospital, Bristol, forthwith.

BROMSGROVE, WORCESTERSHIRE. BARNSLEY HALL HOSPITAL (for Mental and Nervous Diseases). (750 Beds.) Applications are invited for the post of JUNIOR HOSPITAL MEDICAL OFFICER. Excellent opportunities for a young man to study in a modern mental hospital, modern treatments and up-to-date psychiatry. Furnished flat available. Remuneration will be in accordance with the terms and conditions of service issued by the Ministry of Health.

Applications, stating age and experience, together with the names of 3 referees, to the Medical Superintendent.

BROMSGROVE GENERAL HOSPITAL, Worcestershire. (411 Beds.) Applications are invited for the pre-registration post of HOUSE SURGEON at the above Hospital. Post vacant now.

Applications, with the names of 3 referees, to the Hospital Secretary.

BROMSGROVE GENERAL HOSPITAL, Worcestershire. (411 Beds.) Applications are invited for the pre-registration post of HOUSE PHYSICIAN at the above Hospital. Post vacant now.

Applications, with the names of 3 referees, to the Hospital Secretary.

BURTON-ON-TRENT. THE GENERAL HOSPITAL. HOUSE OFFICER (orthopædics) (pre-registration post) required at the above Hospital. Recognised for F.R.C.S.

Applications to Group Secretary as soon as possible.

BURNLEY GENERAL HOSPITAL. (641 Beds.) Senior HOUSE OFFICER (medical). The post offers good all-round experience under Consultant Staff. Good accommodation available for single or married applicant. Post available mid-August.

Applications, with 2 references, to Group Secretary, Burnley and District Hospital Management Committee, Burnley General Hospital.

BURNLEY AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. SENIOR HOUSE OFFICER to Orthopædic and Casualty Departments. Recognised for F.R.C.S. Resident accommodation available. Post available September.

Applications, with the names of 2 referees, to Group Secretary, Burnley General Hospital.

CAMBRIDGE. THE UNITED CAMBRIDGE HOSPITALS. ADDENBROOKE'S HOSPITAL, CAMBRIDGE. HOUSE SURGEON (in Orthopædic Department) for 6 months from early August. Recognised pre-registration service.

Apply to the Secretary immediately, stating age, nationality, qualifications and experience, with dates, and with copies of 3 testimonials.

CAMBRIDGE, ADDENBROOKE'S HOSPITAL. Senior REGISTRAR (non-resident) and REGISTRAR (resident) in Anæsthetics required from 1st October, 1958, and 24th September, 1958, respectively.

Apply, with full particulars and names of 3 referees, to Secretary, Addenbrooke's Hospital, Cambridge, by 25th July, 1958.

CANTERBURY. KENT AND CANTERBURY HOSPITAL. (277 Beds.) Applications are invited for the post of SENIOR HOUSE OFFICER (pathology), which becomes vacant mid-July, 1958, for 1 year. Salary £819 10s. p.a., with National Health Service conditions. Experience in pathology not essential but candidates must have had previous clinical experience.

Applications, stating age, qualifications, together with copies of 2 recent testimonials, to be addressed to the Hospital Secretary at the above Hospital.

CARDIFF. ST. DAVID'S HOSPITAL. Resident OBSTETRICAL HOUSE OFFICER (recognised for M.R.C.O.G.) required in a Maternity Department at above Hospital. Commencing 1st August, 1958.

Form of application from Group Secretary, Cardiff Hospital Management Committee, 44, Cathedral-road, Cardiff.

CARSHALTON, SURREY. QUEEN MARY'S HOSPITAL FOR CHILDREN. (General children's hospital of 550 Beds.) HOUSE PHYSICIAN (Senior House Officer) required, care of acute medical, rheumatism and poliomyelitis beds.

Applications, stating age, qualifications and experience, together with copies of 3 testimonials, should reach the Group Secretary by 19th July, 1958.

CARSHALTON, SURREY. QUEEN MARY'S HOSPITAL FOR CHILDREN. (A general children's hospital of 550 Beds.) RESIDENT MEDICAL REGISTRAR required. Recognised for D.C.H.

Applications, on forms obtainable from the Group Secretary, should be returned by 2nd August, 1958.

CARSHALTON, SURREY. QUEEN MARY'S HOSPITAL FOR CHILDREN. (A general children's hospital of 550 Beds.) HOUSE SURGEON (Senior House Officer) required (general surgery, E.N.T. and orthopædics). Recognised for D.C.H.

Applications, stating age and qualifications, together with 1 recent testimonial and the names of 2 referees, should be submitted to the Group Secretary immediately.

CARSHALTON, SURREY. ST. HELIER HOSPITAL. Locum SENIOR ANÆSTHETIC REGISTRAR required at above Hospital, 14th July for 3 weeks.

Please telephone Establishment Officer at Fairlands 6633.

CHATHAM, KENT. ALL SAINTS' HOSPITAL. Medway AND GRAVESEND HOSPITAL MANAGEMENT COMMITTEE. PÆDIATRIC HOUSE PHYSICIAN required. Post vacant now, recognised for D.C.H.; salary on House Officer scale according to experience.

Applications to Hospital Secretary, giving details of experience, qualifications, age and nationality, with copies of recent testimonials.

CHELTENHAM GENERAL HOSPITAL. (220 Beds.) HOUSE SURGEON required (pre- or post-registration). The post offers a wide experience in general surgery, gynæcology, and orthopædic surgery. Post recognised for the F.R.C.S.

Apply, with names of 2 referees, to the Secretary, General Hospital, Cheltenham.

CHERTSEY, SURREY. ST. PETER'S HOSPITAL. (430 Beds.) ANÆSTHETIC REGISTRAR required. Post recognised for F.F.A. R.C.S. and D.A. Hospital may be visited by arrangement with Physician-Superintendent (Tel. Ottershaw 441).

Application forms from Secretary, Woking and Chertsey Hospital Management Committee, "Huntington," Guildford-road, Chertsey, Surrey. Closing date 22nd July.

CHICHESTER. ST. RICHARD'S HOSPITAL. Applications are invited for the post of HOUSE PHYSICIAN (recognised for pre-registration) for 6 months only in the first instance. Vacant middle of August, 1958.

Applications, stating age, qualifications and experience, and giving names of 2 persons to whom reference may be made, should be sent to the Surgeon-Superintendent.

CHICHESTER. ST. RICHARD'S AND ROYAL WEST SUSSEX HOSPITALS. Applications are invited for the post of RESIDENT OBSTETRIC AND GYNÆCOLOGY SENIOR HOUSE SURGEON, for 6 months in first instance. Obstetrics at St. Richard's (where resident) and gynæcology at both Hospitals. Occasional relief duties at Maternity Hospital, Rustington (50 Beds). Salary £819 10s., less £150 p.a. for residence.

Apply Group Secretary, 184, Broyle-road, Chichester, giving names of 2 referees.

COVENTRY. GULSON HOSPITAL. House Officer in General Surgery (pre-registration). Recognised F.R.C.S. Resident. Vacant July.

Applications to Group Secretary, Coventry and Warwickshire Hospital, Coventry.

COLCHESTER GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications invited for Locum SURGICAL REGISTRAR required from 31st July, 1958, at Essex County Hospital, Colchester.

Applications, with copies of testimonials, to Group Secretary, Colchester Hospital Management Committee, 14, Pope's-lane, Colchester.

COLCHESTER GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications invited for:—

Black Notley Hospital, Braintree, Essex (522 Beds)

Post of SENIOR HOUSE OFFICER for Non-Pulmonary Tuberculosis Unit of approximately 120 Beds, particularly for skeletal and renal tuberculosis; also rheumatoid arthritis cases and spastic children. Recognised for F.R.C.S.

Post of HOUSE PHYSICIAN. Pre-registration or third post. Includes duties in medical and pædiatric wards. Tenable for 6 months.

Post of HOUSE SURGEON. Pre-registration or third post. Includes duties in general surgical and gynæcological wards. Recognised for F.R.C.S. Tenable for 6 months.

Clacton and District Hospital, Clacton-on-Sea, Essex (58 Beds)

Post of SENIOR HOUSE OFFICER. Duties include medical, surgical, and casualty work. Post tenable for 6 months or 1 year.

Applications, with copies of 3 testimonials, to Group Secretary, 14, Pope's-lane, Colchester, Essex.

COLCHESTER, ESSEX. ROYAL EASTERN COUNTIES, HOSPITAL. Applications are invited for the appointment of JUNIOR HOSPITAL MEDICAL OFFICER (Male or Female, resident or non-resident). This Hospital admits mental defectives of both sexes and of all ages and grades. National Health Service salary scale. Excellent facilities exist for study.

Applications, giving full details and with names of 2 referees, to the Group Secretary at Abbeygate House, Colchester.

COLCHESTER, ESSEX. SEVERALLS HOSPITAL. SENIOR HOUSE OFFICER required at the above Mental Hospital. There are excellent opportunities for up-to-date experience and postgraduate work in all branches of psychiatry, including treatment of neurosis. Opportunities will be given at the Hospital for clinical instruction for the D.P.M.

Applications, with particulars and copies of testimonials, or names of referees, to the Medical Superintendent as soon as possible.

CREWE AND DISTRICT MEMORIAL HOSPITAL. (108 Beds—acute, and continuation 32 Beds.) SENIOR HOUSE OFFICER (casualty) required. Approved for F.R.C.S. Now vacant. Modern well-equipped department. Whitley Council salary scale and conditions of service.

Apply immediately, stating age, qualifications, &c., with names of 2 referees, to reach the Group Secretary, South Cheshire Hospital Management Committee, Barony Hospital, Nantwich, Cheshire, not later than 19th July, 1958.

CUCKFIELD HOSPITAL, Cuckfield, near Haywards HEATH. MID SUSSEX HOSPITAL MANAGEMENT COMMITTEE. Vacancies as follows:—

RESIDENT JUNIOR HOUSE PHYSICIAN. Post approved for pre-registration, but fully registered practitioners may apply. Vacant 26th July.

RESIDENT JUNIOR HOUSE SURGEON (Orthopædic and Traumatic Unit). Post vacant now.

Apply stating age, nationality, qualifications and experience, with names of 2 referees, to Hospital Secretary in both cases.

DERBY. DERBYSHIRE CHILDREN'S HOSPITAL. (86 Beds.) Pædiatrics. Applications are invited for the post of SENIOR HOUSE OFFICER (pædiatrics) vacant 1st September, 1958, tenable for 6 months. Duties mainly medical but include some surgery. Post recognised for D.C.H.

Applications, with names of 2 referees, to be sent as soon as possible to Secretary.

DERBY. DERBYSHIRE CHILDREN'S HOSPITAL. (86 Beds.) Applications invited for post of HOUSE OFFICER or SENIOR HOUSE OFFICER (pædiatrics), vacant 16th July, 1958, tenable for 6 months. Duties mainly surgical, but include some medicine. Post recognised for D.C.H. and is open to pre-registration graduates.

Applications, with names of 2 referees, to be sent as soon as possible to Secretary.

DERBY. DERBYSHIRE HOSPITAL FOR WOMEN, FRIAR GATE. HOUSE SURGEONS (pre-registration) or SENIOR HOUSE OFFICERS (gynæcology) required on 21st August, 1958, and 1st September, 1958. Recognised for M.R.C.O.G. in gynæcology only.

Apply, stating full details, with copies of 2 recent testimonials, to Hospital Secretary, Derbyshire Hospital for Women.

DERBY. DERBYSHIRE ROYAL INFIRMARY. (416 Beds.) HOUSE PHYSICIAN (pre-registration) or SENIOR HOUSE OFFICER (general medicine), vacant late August.

Apply, stating full details with copies of 2 testimonials, to Secretary.

DERBY. DERBYSHIRE ROYAL INFIRMARY. (416 Beds.) SENIOR HOUSE OFFICER in Clinical Pathology. Vacant 26th August. Preference will be given to an applicant who is studying for a higher quaidfication in any branch of medicine, not necessarily pathology. The holder is expected to attend clinical work in the Royal Infirmary and sometimes in associated hospitals.

Apply, stating full details and 2 names for reference, to Secretary.

DERBY. KINGSWAY HOSPITAL. (912 Beds. Recognised for D.P.M.) SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time RESIDENT or NON-RESIDENT REGISTRAR (psychiatry) required 24th August. Facilities for postgraduate study in conjunction with Sheffield University available. Appointment for 1 year in first instance.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 21st July, 1958, giving age, nationality, qualifications, present and previous appointments with dates, naming 3 referees.

DORCHESTER. DORSET COUNTY HOSPITAL. House SURGEON (Male or Female) required for resident, pre-registration post becoming vacant early August. Recognised for F.R.C.S. examination and tenable for 6 months.

Applications, stating age, qualifications, together with copy testimonials, to Group Secretary, West Dorset Hospital Management Committee, Damers-road, Dorchester, Dorset.

DONCASTER ROYAL INFIRMARY. (330 Beds.) Applications are invited for the post of HOUSE PHYSICIAN (Intern or Senior House Officer).

Applications, with particulars of experience and copies of 2 recent testimonials, to the Group Secretary, Doncaster Hospital Management Committee, at Doncaster Royal Infirmary.

DRIFFIELD, YORKSHIRE. EAST RIDING GENERAL HOSPITAL. (247 Beds.) HOUSE SURGEON (first, second or third post). Vacant now. General surgery, casualty and some orthopædics. Approved pre-registration post. Fully registered practitioners may apply. Married quarters may be available.

Applications to Group Secretary, Westwood Hospital, Beverley, Yorkshire.

DRIFFIELD, YORKSHIRE. EAST RIDING GENERAL HOSPITAL. (247 Beds.) JUNIOR HOUSE PHYSICIAN, vacant now. Approved pre-registration post, but fully registered practitioners may apply. Duties to include geriatrics and acute medicine. Good general experience. Married quarters may be available.

Apply Group Secretary, Westwood Hospital, Beverley, Yorkshire.

DUNFERMLINE. NORTHERN HOSPITAL. (General medical—101 Beds.) WEST FIFE HOSPITALS BOARD OF MANAGEMENT. HOUSE PHYSICIAN required to commence 1st October; 1 of 2 pre-registration service posts. Substantial turnover of inpatients and usual outpatient sessions. Resident staff consists of 1 Junior Hospital Medical Officer and 2 House Physicians.

Applications, with copy references, to the Medical Superintendent.

DURHAM. COUNTY HOSPITAL. (116 Beds.) **Resident** HOUSE SURGEON required in Orthopædics and Casualty. Post recognised for pre-registration purposes. This post offers facilities for good and varied experience in a busy orthopædic and accident hospital which serves a wide mining and industrial area.

Apply, giving age, experience and names of 2 referees, to the Group Secretary, Dryburn Hospital, Durham.

DURHAM. COUNTY HOSPITAL. (116 Beds.) **Resident** SENIOR HOUSE OFFICER in Orthopædics. The County Hospital is the main Orthopædic and Accident Hospital in a busy mining and industrial area. Experience can be obtained in all branches of orthopædics.

Applications, with particulars of previous experience and names of 2 referees, to Group Secretary, Dryburn Hospital, Durham.

DURHAM. DRYBURN HOSPITAL. (309 Beds.) **Senior** HOUSE OFFICER in Anæsthetics. Post recognised for D.A. and F.F.A.R.C.S. Previous experience in anæsthetics is not essential. Vacant 1st August, 1958.

Apply, with names and addresses of 2 referees, to Group Secretary, Dryburn Hospital, Durham.

EAST ANGLIAN REGIONAL HOSPITAL BOARD. ANÆSTHETIC REGISTRAR, West Norfolk and King's Lynn Hospital, King's Lynn (146 Beds). Post provides wide experience and recognised for D.A. Single accommodation available now. Married quarters will be available in approximately 6 months. Appointment for 1 year, renewable for second year.

Applications, stating age, experience, and the names of 3 referees, to Board's Senior Administrative Medical Officer, 117, Chesterton-road, Cambridge, by 21st July, 1958. Candidates invited to visit Hospital by direct arrangement with Hospital Management Committee Secretary at the Hospital.

EAST ANGLIAN REGIONAL HOSPITAL BOARD. REGISTRAR in Geriatrics, Ipswich and East Suffolk Hospital Group. New area service in course of development under Consultant Physician in Geriatrics. Duties at Unit in Ipswich and East Suffolk Hospital and other hospitals in the area. Appointment for 1 year, renewable for second year.

Applications, stating age, experience, and the names of 3 referees, to Board's Senior Administrative Medical Officer, 117, Chesterton-road, Cambridge, by 28th July, 1958. Candidates invited to visit by direct arrangement with Hospital Management Committee Secretary, Ipswich and East Suffolk Hospital, Anglesea-road Wing, Ipswich.

EBBW VALE GENERAL HOSPITAL. (General beds 71, maternity 15.) Applications are invited for the vacancy of JUNIOR HOSPITAL MEDICAL OFFICER. Staff comprises Resident Consultant Surgeon, visiting Orthopædic, Gynæcological and Ophthalmic Surgeons, and Resident House Officer. Appointment shall be for a period not exceeding 4 years.

Apply, with full details and references, to Group Secretary, North Monmouthshire Hospital Management Committee, Nevill Hall Hospital, Abergavenny, Mon.

ENFIELD, MIDDLESEX. CHASE FARM HOSPITAL. RESIDENT HOUSE PHYSICIAN (approved pre-registration). Vacant 30th August, 1958. General medical duties. 6 months' appointment.

Applications in own handwriting, with copies of testimonials, to the Group Secretary, Enfield Group Hospital Management Committee, at Chase Farm Hospital.

ENFIELD, MIDDLESEX. CHASE FARM HOSPITAL. RESIDENT HOUSE SURGEON. Pre-registration post. Vacant 3rd September, 1958. Duties with General Surgical Unit, doing some genitourinary work. Post recognised by the Royal College of Surgeons. 6 months' appointment.

Applications, with the names and addresses of 2 referees, to the Group Secretary, Enfield Group Hospital Management Committee, at Chase Farm Hospital.

ENFIELD, MIDDLESEX. CHASE FARM HOSPITAL. Appointment of RESIDENT HOUSE SURGEON (third post). Vacant 1st August, 1958. Post provides experience and duties in both general surgery and orthopædics. 6 months' appointment. Post recognised for F.R.C.S. by the Royal College of Surgeons.

Applications, with the names and addresses of 2 referees, to the Group Secretary, Enfield Group Hospital Management Committee, at Chase Farm Hospital.

ENFIELD. WAR MEMORIAL HOSPITAL, Chase Side, ENFIELD, MIDDLESEX. RESIDENT SENIOR HOUSE OFFICER required immediately for general medical and surgical duties in acute general hospital of 61 Beds. 12-month appointment.

Applications, with names and addresses of 2 referees, to the Group Secretary, Enfield Group Hospital Management Committee, Chase Farm Hospital, The Ridgeway, Enfield, Middlesex.

EDGWARE GENERAL HOSPITAL, Edgware, Middlesex. (704 Beds.) Locum CASUALTY REGISTRAR required at above Hospital from 4th to 17th August, 1958, inclusive.

Apply immediately to Medical Administrator, telephone EDGware 2381.

EPSOM DISTRICT HOSPITAL, Dorking-road, Epsom, SURREY. RESIDENT HOUSE SURGEON required 12th August for General Surgery. Pre-registration post recognised for F.R.C.S.

Applications, stating age, qualifications and experience with copies of 2 recent testimonials, should be sent as soon as possible to Group Secretary at above address.

EPSOM DISTRICT HOSPITAL, Dorking-road, Epsom, SURREY. RESIDENT HOUSE SURGEON required 28th July for Orthopædic, E.N.T. and Eye Departments. Pre-registration post recognised for F.R.C.S.

Applications, stating age, qualifications and experience, with copies of 2 recent testimonials, should be sent as soon as possible to Group Secretary at above address.

EXETER. ROYAL DEVON AND EXETER HOSPITAL. Applications are invited from registered medical practitioners for the appointment of SENIOR HOUSE OFFICER (E.N.T. Department—30 Beds). Vacant now. The post is recognised for the F.R.C.S. examination.

Applications, with copies of 2 recent testimonials, to the Hospital Secretary.

GLASGOW, N.1. STOBHILL GENERAL HOSPITAL MEDICAL UNIT. (97 Beds.) Applications are invited for the post of HOUSE OFFICER (recognised for pre-registration) for the 6 months beginning 1st August, 1958, and should be addressed to the Medical Superintendent, giving the names of 2 referees.

GLASGOW, N.1. STOBHILL GENERAL HOSPITAL DERMATOLOGY UNIT. (118 Beds.) Applications are invited for the post of HOUSE OFFICER (recognised for pre-registration) for the 6 months beginning 1st August, 1958, and should be addressed to the Medical Superintendent, giving the names of 2 referees.

GLASGOW, S.W.1. SOUTHERN GENERAL HOSPITAL. SENIOR HOUSE OFFICER in Surgery.

Write immediately to Secretary, Board of Management for Glasgow South-Western Hospitals, 1301, Govan-road, Glasgow, S.W.1, naming 2 referees.

GLASGOW, S.W.1. SOUTHERN GENERAL HOSPITAL. SENIOR HOUSE OFFICER and JUNIOR HOUSE OFFICER for the University Department of Psychological Medicine. This is a busy and progressive unit situated in a large General Hospital and offers excellent opportunity for experience and research.

Write immediately to Secretary, Board of Management for Glasgow South-Western Hospitals, 1301, Govan-road, Glasgow, S.W.1, naming 2 referees.

GRANTHAM AND KESTEVEN GENERAL HOSPITAL. (118 Beds.) RESIDENT HOUSE PHYSICIAN (Senior House Officer or Pre-registration Intern). General medical and paediatric. Post vacant 17th July, 1958.

Applications, with details of experience, &c., and names of 2 referees, to Secretary, 101, Manthorpe-road, Grantham, Lincs.

GRANTHAM AND KESTEVEN GENERAL HOSPITAL. (117 Beds. Recognised for training for F.R.C.S.) SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time RESIDENT SURGICAL REGISTRAR required. Appointment for 1 year in first instance.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 21st July, 1958, giving age, nationality, qualifications, present and previous appointments with dates, naming 3 referees.

GRAVESEND AND NORTH KENT HOSPITAL, GRAVESEND, KENT. MEDWAY AND GRAVESEND HOSPITAL MANAGEMENT COMMITTEE. RESIDENT SURGICAL OFFICER (Senior House Officer grade) required for new post. Excellent experience in busy general hospital. Salary £819 10s., less £150 p.a. for residential emoluments.

Applications, stating age, qualifications, experience and nationality, to the Hospital Secretary.

GRIMSBY HOSPITAL MANAGEMENT COMMITTEE. 2 HOUSE PHYSICIANS (pre-registration) required in July, 1 for Scartho Road Hospital and 1 for Grimsby General Hospital. Units of 35 and 46 Beds respectively. Medical library and reading facilities available.

Applications for either post, with names of 2 referees, to the Hospital Secretary, Grimsby General Hospital, Grimsby.

GRIMSBY. SPRINGFIELD HOSPITAL. (202 Beds.) SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time RESIDENT or NON-RESIDENT REGISTRAR (chest and infectious diseases) required. House available. There is a Thoracic Unit at the Hospital. Some clinic work would be undertaken under Consultant supervision. Appointment for 1 year in first instance.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 21st July, 1958, giving age, nationality, qualifications, present and previous appointments with dates, naming 3 referees.

HARROW CHEST CLINIC, 199, Station-road, Harrow, MIDDLESEX. NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. Whole-time REGISTRAR in Chest Diseases required at above Clinic. Duties will include supervision of beds at Edgware General Hospital. Good training in general medicine essential and some experience in chest diseases desirable. Clinic may be visited by direct appointment.

Application forms obtainable from and returnable to Group Secretary, Hendon Group Hospital Management Committee, Edgware General Hospital, Edgware, Middlesex, by 26th July, 1958.

GREAT YARMOUTH AND GORLESTON GENERAL HOSPITAL, Dene Side, GREAT YARMOUTH. (134 Beds.) HOUSE PHYSICIAN required, House Officer or Senior House Officer status. Post vacant 1st August, 1958, recognised for pre-registration service. Membership of a Medical Defence Society is a condition of appointment.

Applications, giving full details with names of 2 referees, to Hospital Secretary.

HALIFAX AREA HOSPITALS MANAGEMENT COMMITTEE. JUNIOR HOSPITAL MEDICAL OFFICER wanted for duties in the wards for chest cases at the Northowram Hall Hospital, Halifax, and the Outpatients' Chest Clinic at the Royal Halifax Infirmary. Approximately 20 non-tuberculous chest patients in hospital and 75 tuberculous. Self-contained flat in good residential accommodation at Hospital. Vacant now.

Applications to be forwarded to the Group Secretary at Royal Halifax Infirmary, Halifax.

HALIFAX. ROYAL HALIFAX INFIRMARY. (301 Beds.) SENIOR HOUSE OFFICER in General Surgery required. Post vacant on 1st August, 1958. Salary £819 10s. p.a. with deduction of £150 p.a. for board-residence, &c.

Applications to the Group Secretary.

HASLEMERE AND DISTRICT HOSPITAL. (83 Beds.) GUILDFORD GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners for the post of SENIOR HOUSE OFFICER (surgical with charge of 12 acute medical beds). Duties to commence 10th September, 1958. Valuable experience in general and emergency surgery, orthopædic, E.N.T., gynæcological, children and casualty work. Cottage available October.

Applications to Hospital Secretary, Haslemere and District Hospital, Haslemere, Surrey, immediately, with names of 3 referees.

HASTINGS. ROYAL EAST SUSSEX HOSPITAL. (150 Beds.) HOUSE SURGEON. Pre-registration post for general surgery and urology required at this acute hospital (surgical) immediately.

Applications, with names of 2 referees, to Administrator.

HASTINGS. ROYAL EAST SUSSEX HOSPITAL. (150 Beds.) Locum HOUSE SURGEON required. Pre-registration or Senior House Officer, according to experience.

Apply to Hospital Administrator.

HASTINGS. ROYAL EAST SUSSEX HOSPITAL. (150 Beds.) Applications are invited for the post of CASUALTY AND ORTHOPÆDIC HOUSE SURGEON, 1 of 2 similar posts, graded Senior House Officer, for the Royal East Sussex Hospital, Hastings. Modern department. Post vacant 9th August, 1958.

Applications, with names of 2 referees, to the Administrator at the above Hospital.

HASTINGS. ROYAL EAST SUSSEX HOSPITAL. (150 Beds.) Applications are invited for the post of HOUSE SURGEON at the Royal East Sussex Hospital, Hastings. Pre-registration post recognised for F.R.C.S. Vacant 26th July, 1958. The Hospital is pleasantly situated facing the sea and is the main surgical hospital in the Hastings Group. Post offers excellent experience.

Applications, with names of 2 referees, to the Administrator.

HEMEL HEMPSTEAD, HERTFORDSHIRE. WEST HERTS HOSPITAL. 2 HOUSE SURGEONS (pre-registration) required.

Applications, giving full details and 2 names for reference, should be sent to the Hospital Secretary as soon as possible.

HERTFORD COUNTY HOSPITAL. (171 Beds. Hospital situated 21 miles from London.) Applications are invited for appointment of RESIDENT HOUSE PHYSICIAN (Male or Female), second post held. Recognised pre-registration post. Preference given to applicants who have held resident surgical or medical posts in general hospital. Duties to commence 1st August, 1958.

Applications to Group Secretary, Hertford Hospital Management Committee, County Hospital, Hertford, Herts.

HIGH WYCOMBE, BUCKINGHAMSHIRE. WAR MEMORIAL HOSPITAL. (100 Beds.) SENIOR RESIDENT HOUSE PHYSICIAN required immediately.

Apply, with copies of testimonials or names of 2 referees, to the Secretary.

HIGH WYCOMBE WAR MEMORIAL HOSPITAL, BUCKINGHAMSHIRE. HOUSE SURGEON required for General Surgery and E.N.T.

Apply to Secretary.

HITCHIN, HERTFORDSHIRE. LISTER HOSPITAL. RESIDENT HOUSE SURGEON post now vacant. Recognised as pre-registration post and for F.R.C.S.

Applications, stating age, nationality, qualifications and experience, together with copies of 3 recent testimonials, to be sent to the Medical Administrator, Lister Hospital.

HORNCHURCH. ST. GEORGE'S HOSPITAL. Junior HOSPITAL MEDICAL OFFICER (resident) required from approximately 1st September next at this Hospital which accommodates 404 chronic sick patients. The post offers excellent geriatric experience.

Applications should be forwarded to the Secretary, Romford Group Hospital Management Committee, Oldchurch Hospital, Romford, as soon as possible.

HULL. VICTORIA HOSPITAL FOR SICK CHILDREN, Park-street. HOUSE SURGEON required on 1st August, 1958. Pre-registration or registration post. Recognised for D.C.H. An interesting and varied post which includes outpatient and casualty work.

Applications, together with details of experience, testimonials, &c., to the Hospital Secretary.

HULL. KINGSTON GENERAL HOSPITAL. (419 Beds.) HULL A GROUP HOSPITAL MANAGEMENT COMMITTEE. HOUSE SURGEON (pre-registration post). Resident, and tenable for 6 months. This post includes gynæcology and general surgery.

Applications, with 2 recent testimonials, to the Hospital Secretary.

HULL. KINGSTON GENERAL HOSPITAL. (419 Beds.) HULL A GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of RESIDENT HOUSE PHYSICIAN (pre-registration post). Vacant mid-July.

Applications, with 2 recent testimonials, to the Hospital Secretary.

HUDDERSFIELD. MILL HILL HOSPITAL. (164 Beds.) HUDDERSFIELD HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of RESIDENT MEDICAL OFFICER (Junior Hospital Medical Officer grade, £852 10s.–£55–£1182 10s. p.a.) at above Hospital. The present allocation of beds is 28 for infectious diseases and 136 for geriatric patients.

Applications, together with copies of 3 recent testimonials, to be addressed to the undersigned as soon as possible.

H. J. JOHNSON, Group Secretary,
Huddersfield Hospital Management Committee.
The Royal Infirmary, Huddersfield.

HUDDERSFIELD ROYAL INFIRMARY. (285 Beds.) HUDDERSFIELD HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from provisionally registered medical practitioners for the post of HOUSE PHYSICIAN to commence duties immediately. Salary in accordance with national scale.

Applications, together with copies of 3 recent testimonials, to be addressed to the undersigned as soon as possible.

H. J. JOHNSON, Group Secretary,
Huddersfield Hospital Management Committee.
The Royal Infirmary, Huddersfield.

HUDDERSFIELD ROYAL INFIRMARY. (285 Beds.) HUDDERSFIELD HOSPITAL MANAGEMENT COMMITTEE. HOUSE SURGEON required to commence duty on 6th August, 1958. The post is recognised as a pre-registration appointment and for the F.R.C.S. Salary in accordance with national scale.

Applications, together with copies of 3 recent testimonials, to be addressed to the undersigned as soon as possible.

H. J. JOHNSON, Secretary to the Management Committee.
The Royal Infirmary, Huddersfield.

HUNTINGDON COUNTY HOSPITAL. Applications are invited for the post of HOUSE OFFICER (surgical) now vacant. Post recognised for pre-registration purposes.

Apply, with full particulars and names of 2 referees, to Secretary. County Hospital, Huntingdon.

ILKLEY, YORKSHIRE. MENSTON (MENTAL) HOSPITAL. Locum Tenens JUNIOR HOSPITAL MEDICAL OFFICER required immediately for holiday relief. Residential accommodation available for single person.

Applications, stating age, qualifications and experience and names of 2 referees, to Physician-Superintendent.

IPSWICH. ST. HELEN'S HOSPITAL. (129 Beds for infectious diseases, pulmonary tuberculosis, long-stay orthopædics and geriatrics. The area Chest Clinic is in the Hospital.) HOUSE PHYSICIAN required (post-registration appointment). Accommodation available for married man.

Applications to JOHN WILLIAMS, Group Secretary, Ipswich Group Hospital Management Committee, at the Ipswich and East Suffolk Hospital (Anglesea-road Wing), Ipswich.

KETTERING AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners for the appointment of SENIOR HOUSE OFFICER to the Geriatric Unit in this area. There are 160 active beds in the unit in 3 hospitals. Post vacant 14th August, 1958. Residential accommodation available. National scale of salary.

Applications, together with the names and addresses of 2 referees, to the Group Secretary, Central Administration Offices, General Hospital, Kettering.

KIDDERMINSTER AND DISTRICT GENERAL HOSPITAL, WORCESTERSHIRE. (112 Beds.) Applications are invited for the pre-registration post of HOUSE SURGEON at the above Hospital. Post vacant now.

Applications, with the names of 3 referees, to the Hospital Secretary.

KINGSTON HOSPITAL, Wolverton-avenue, Kingston-UPON-THAMES. KINGSTON GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from suitably qualified medical officers for the post of SENIOR HOUSE OFFICER (general surgery)—2 posts which are available on 1st September, 1958. The posts are recognised for F.R.C.S. purposes.

Applications, stating age, qualifications and experience with 2 testimonials, should reach the Physician-Superintendent of the Hospital within 7 days of the appearance of this advertisement.

KINGSTON HOSPITAL, Wolverton-avenue, Kingston-UPON-THAMES. KINGSTON GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from suitably qualified medical officers for the post of SENIOR HOUSE OFFICER (orthopædic and casualty) which is available on 1st September, 1958. The post is recognised in casualty for F.R.C.S. purposes.

Applications, stating age, qualifications and experience, with 2 recent testimonials, should reach the Physician-Superintendent of the Hospital within 7 days of the appearance of this advertisement.

KINGSTON HOSPITAL, Wolverton-avenue, Kingston-UPON-THAMES. KINGSTON GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from suitably qualified medical officers for the post of HOUSE OFFICER (general surgery)—2 posts (pre-registration) which are available on 1st August, 1958.

Applications, stating age, qualifications and experience, with 2 recent testimonials, should reach the Physician-Superintendent of the Hospital as soon as possible.

LEEDS. THE UNITED LEEDS HOSPITALS. THE GENERAL INFIRMARY AT LEEDS. Applications are invited for the post of REGISTRAR in the Department of Psychiatry (Leeds University) to work at the General Infirmary at Leeds. Some previous experience of psychiatry necessary. Facilities are available for attendance at the course for the Leeds University D.P.M. or for preparation for a higher degree.

Applications, including the names of 3 referees, to be sent to the Sub-Dean, School of Medicine, Leeds, 2, by not later than 28th July, 1958.

LEEDS (near). WOODLANDS ORTHOPÆDIC HOSPITAL, RAWDON, near LEEDS. (112 Beds.) SENIOR HOUSE OFFICER (resident) required. Post vacant 1st October, 1958.

Applications, stating age and experience, with copies of 2 testimonials, to the Secretary, The Royal Infirmary, Bradford, 9, Yorkshire.

LEAMINGTON SPA. WARNEFORD GENERAL HOSPITAL. (197 Beds.) RESIDENT HOUSE SURGEON (general surgery). Post vacant. Recognised for pre-registration and F.R.C.S. Post provides excellent experience, good accommodation available.

Applications, with 2 recent testimonials, to Hospital Secretary.

LINCOLN COUNTY HOSPITAL, Sewell-road, Lincoln. (200 Beds.) Applications are invited from Men and Women for 2 posts of RESIDENT HOUSE SURGEON. These are approved pre-registration posts which will be vacant on 1st August, 1958. The duties are with General Surgeons. If satisfactory, candidates will be appointed for a second 6 months as House Physicians.

Applications, with copy testimonials, should be sent to the Group Secretary, Lincoln County Hospital, as soon as possible.

LINCOLN COUNTY HOSPITAL, Sewell-road, Lincoln. (200 Beds.) Applications are invited from Men and Women for the post of RESIDENT HOUSE PHYSICIAN. This is an approved pre-registration post which will be vacant on 1st August, 1958. If satisfactory, candidates will be appointed for a second 6 months as House Surgeons.

Applications, with copy testimonials, should be sent to the Group Secretary, Lincoln County Hospital, as soon as possible.

LIVERPOOL, 9. AINTREE HOSPITAL. Fazakerley GROUP OF HOSPITALS MANAGEMENT COMMITTEE. RESIDENT SENIOR HOUSE OFFICER (surgical). Applications are invited from registered medical practitioners. The Hospital is for the treatment of pulmonary and non-pulmonary tuberculosis, and is a main centre for thoracic surgery and has an Orthopædic Department. Salary will be in accordance with terms and conditions of service for hospital medical staff.

Applications, endorsed "Resident Senior House Officer", to be submitted immediately to the Physician-Superintendent.

LLWYNYPIA HOSPITAL, Llwynypia, Rhondda. Pontypridd AND RHONDDA HOSPITAL MANAGEMENT COMMITTEE. HOUSE OFFICER (medicine) required immediately. The person appointed will be required to undertake duties at the Llwynypia Hospital (40 acute medical beds and 78 chronic sick beds), Glyncornel Hospital (56 chronic sick beds), and Tyntyla Isolation Hospital (42 Beds).

Applications, stating age, qualifications and experience, together with copies of 2 recent testimonials, to be sent immediately to the Group Secretary, Pontypridd and Rhondda Hospital Management Committee, Courthouse-street, Pontypridd.

MAIDSTONE. WEST KENT GENERAL HOSPITAL. (141 Beds.) MID-KENT HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the pre-registration post of HOUSE SURGEON. 6 months' appointment. Vacant now. Recognised for F.R.C.S. Salary at the rate of £467 10s.–£577 10s. p.a. A deduction at the rate of £125 a year is made for board and lodging, and other services provided.

Applications should be forwarded, as soon as possible, to the Administrative Officer at the Hospital.

MANSFIELD AND DISTRICT HOSPITAL. (206 Beds. Recognised training hospital for D.A. and F.F.A.R.C.S.) SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time RESIDENT REGISTRAR (anæsthetics) required 1st September. Appointment for 1 year in first instance.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 21st July, 1958, giving age, nationality, qualifications, present and previous appointments with dates, naming 3 referees.

MANCHESTER. BOOTH HALL CHILDREN'S HOSPITAL, BLACKLEY, MANCHESTER, 9. (380 Beds. Recognised for D.C.H.)

RESIDENT SENIOR HOUSE OFFICER (surgical). Duties orthopædic and E.N.T. Post vacant 1st August.

Applications, giving names and addresses of 2 referees, to be sent to Group Secretary, from whom further particulars may be obtained.

HOUSE OFFICER (surgical), pre- or post-registration. Duties mainly general surgery and neurosurgery. Post vacant.

Applications immediately, with usual particulars and copies of 2 recent testimonials, to Group Secretary.

MANCHESTER REGIONAL HOSPITAL BOARD. Applications are invited for the whole-time post of REGISTRAR in Chest Diseases in Ashton, Hyde and Glossop Group and Oldham and District Group of hospitals. The post offers wide experience in both outpatient clinics and pulmonary hospitals.

Applications, stating age, nationality, qualifications and experience, with copies of 2 references, should be forwarded to the Group Secretary, Ashton-under-Lyne General Hospital Ashton-under-Lyne, Lancashire, as soon as possible.

MANCHESTER REGIONAL HOSPITAL BOARD. South MANCHESTER HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners for the post of RESIDENT SURGICAL OFFICER (Registrar grade) at Wythenshawe Hospital. The post will include responsibility for general surgical beds, and is recognised by the Royal College of Surgeons.

Applications, stating age, qualifications, present post, experience and names of 2 referees, to the Group Secretary, Withington Hospital, Manchester, 20.

MANCHESTER REGIONAL HOSPITAL BOARD. Applications are invited for the whole-time resident post of REGISTRAR in Obstetrics and Gynæcology in the Ashton, Hyde and Glossop Group of hospitals with main duties at Ashton-under-Lyne General Hospital. The post is recognised for the purpose of the M.R.C.O.G.

Applications, with copies of 2 references, to the Group Secretary, Ashton, Hyde and Glossop Hospital Management Committee, Ashton-under-Lyne General Hospital, Ashton-under-Lyne, Lancs.

MANCHESTER. SOUTH MANCHESTER HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of SENIOR HOUSE OFFICER (anæsthetics) with duties in the South Manchester Group. This post is recognised by the Royal College of Surgeons for the F.F.A. R.C.S. and for the D.A.

Applications, stating age, present post, experience and the names of 2 referees, to be forwarded immediately to the Group Secretary, Withington Hospital, Manchester, 20.

MANCHESTER. UNITED MANCHESTER HOSPITALS. MANCHESTER ROYAL EYE HOSPITAL. Applications are invited for the post of SENIOR HOUSE OFFICER.

Application forms may be obtained from the undersigned.

H. R. NORTH, General Superintendent.
Manchester Royal Eye Hospital.

MANCHESTER. UNITED MANCHESTER HOSPITALS. MANCHESTER ROYAL EYE HOSPITAL. Applications are invited for the post of RESIDENT SURGICAL OFFICER (Registrar grade).

Application forms may be obtained from the undersigned.

H. R. NORTH, General Superintendent.
Manchester Royal Eye Hospital.

MANCHESTER. UNITED MANCHESTER HOSPITALS. MANCHESTER ROYAL INFIRMARY, MANCHESTER, 13. REGISTRAR in the Department of Hæmatology, vacant on 1st October, 1958. Whole-time, non-resident appointment for 12 months, renewable. The post is mainly clinical in character, involving ward and general outpatient clinic duties.

Application form, obtainable from the Secretary, to be returned by 23rd July, 1958.

MANCHESTER. UNITED MANCHESTER HOSPITALS, MANCHESTER ROYAL INFIRMARY, MANCHESTER, 13. 2 SENIOR HOUSE OFFICERS to General Medical Units, to commence on 1st October, 1958. Whole-time, non-resident posts, tenable for 6 months, renewable for a second and possibly a third 6 months.

Application form, obtainable from the Secretary, to be returned by 23rd July, 1958.

MANCHESTER, 23. WYTHENSHAWE HOSPITAL. SOUTH MANCHESTER HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of RESIDENT CLINICAL PATHOLOGIST (Senior House Officer grade). The post offers opportunity for training in all branches of pathology. Previous experience is not required.

Apply, with full details and the names of 2 referees, to the Group Secretary, Withington Hospital, Manchester, 20.

MEXBOROUGH. MONTAGU HOSPITAL AND ANNEXE. (198 Beds.) Locum SENIOR HOUSE OFFICER (casualty and orthopædics). £150 p.a. residential emoluments.

Applications to the Secretary to the Committee, "Fern Bank", Doncaster-road, Rotherham.

MEXBOROUGH. MONTAGU HOSPITAL AND ANNEXE (168 Beds and 30 Beds.) RESIDENT HOUSE SURGEON.

Applications to the Secretary, Hospital Management Committee, "Fern Bank," Doncaster-road, Rotherham.

MEXBOROUGH. MONTAGU HOSPITAL AND ANNEXE. (168 Beds and 30 Beds.) RESIDENT HOUSE PHYSICIAN.

Applications to the Secretary, Hospital Management Committee, "Fern Bank," Doncaster-road, Rotherham.

MIDDLESBROUGH. NORTH ORMESBY HOSPITAL. (184 Beds.) SOUTH TEES-SIDE HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of HOUSE SURGEON for Surgical Team No. 1 at the above Hospital. The post is recognised for pre-registration service under the Medical Act, 1950.

Applications, stating age, qualifications, and experience, and giving names for reference, should be addressed to the Hospital Secretary.

MIDDLESBROUGH. NORTH ORMESBY HOSPITAL. SOUTH TEES-SIDE HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of SENIOR HOUSE OFFICER (gynæcology) at the above Hospital which will be vacant about the middle of July. The post is recognised for the R.C.O.G. examinations.

Applications, stating full details and giving names for reference, should be addressed to the Hospital Secretary.

NEWCASTLE GENERAL HOSPITAL. (800 Beds.) The following resident post becomes vacant 7th July, 1958. HOUSE SURGEON, Accident and Admission Department (recognised for F.R.C.S. diploma). This post is recognised for the purpose of pre-registration service and applications will be accepted from students on the point of taking their qualifying examination.

Applications, with names and addresses of 2 referees, should be sent to the Secretary, Newcastle General Hospital, Westgate-road, Newcastle upon Tyne, 4, as soon as possible.

NEWCASTLE REGIONAL HOSPITAL BOARD. Special AREA COMMITTEE FOR CUMBERLAND AND NORTH WESTMORLAND. REGISTRAR in Ophthalmology. Main duties at the Cumberland Infirmary, Carlisle, also duties at the Dumfries and Galloway Royal Infirmary. Single accommodation at Cumberland Infirmary.

Applications, with names of up to 3 referees, to Senior Administrative Medical Officer, 72, Warwick-road, Carlisle, within 14 days.

NEWCASTLE. THE UNITED NEWCASTLE UPON TYNE HOSPITALS. Applications are invited for the whole-time non-resident appointment of SENIOR REGISTRAR in the Department of Psychological Medicine at the Royal Victoria Infirmary under the direction of the Professor of Psychological Medicine. Applicants should possess either a Diploma in Psychological Medicine or a higher qualification in general medicine and psychiatric experience. The appointment is for 1 year in the first instance and will be subject to the terms and conditions of service of hospital medical staff in the National Health Service.

Applications, giving full details and the names and addresses of 3 referees, should be sent to the undersigned within 2 weeks of the appearance of this advertisement.

A. W. SANDERSON, House Governor and Secretary.
Royal Victoria Infirmary, Newcastle upon Tyne.

NEWCASTLE. THE UNITED NEWCASTLE UPON TYNE HOSPITALS. Applications are invited for the whole-time appointment of SENIOR REGISTRAR in the Department of Anæsthetics. The post, which is non-resident except for rotational emergency duty, offers certain facilities for laboratory and clinical investigation. Applicants should have had considerable experience in anæsthesia and should hold the F.F.A. R.C.S. or the D.A. The appointment is subject to terms and conditions of service of hospital medical staff in the National Health Service.

Applications, giving full particulars and the names and addresses of 3 referees, should be sent to the undersigned within 2 weeks of the appearance of this advertisement.

A. W. SANDERSON, House Governor and Secretary.

Royal Victoria Infirmary, Newcastle upon Tyne.

NEWMARKET GENERAL HOSPITAL, Suffolk. Applications are invited for the post of HOUSE PHYSICIAN now vacant. Duties include house charge of general medical and pulmonary tuberculosis beds. The post is recognised for pre-registration, is resident and tenable for 6 months. Salary in accordance with national scale.

Applications, with 3 recent testimonials, to Medical Superintendent.

NORTHAMPTON (near). CREATON HOSPITAL. Applications are invited from suitably qualified medical practitioners for the post of SENIOR HOUSE OFFICER. The Hospital has 138 Beds, and is for the treatment of both pulmonary and non-pulmonary tuberculosis. There is a major thoracic surgical unit for tuberculosis and non-tuberculous diseases of the chest.

Applications, stating age, experience and qualifications, together with the names and addresses of 2 referees, should be sent to the Secretary, Northampton and District Hospital Management Committee, General Hospital, Northampton, within 7 days of the appearance of this advertisement.

NORTHWOOD, PINNER AND DISTRICT HOSPITAL, Pinner-road, NORTHWOOD, MIDDLESEX. A VACANCY has arisen on the General Practitioner staff of the above Hospital. The successful candidate will be required to act as Duty Officer on a rota basis with other members of the staff.

Applications should be sent to the Group Secretary, Harefield and Northwood Group Hospital Management Committee, Mount Vernon Hospital, Northwood, Middlesex, not later than 19th July, 1958.

NORWICH. NORFOLK AND NORWICH HOSPITAL. Applications are invited for the following appointments vacant 1st August, 1958:—

SENIOR CASUALTY OFFICER AND HOUSE SURGEON to the Septic Block. Senior House Officer status. 2 Casualty Officers employed in the Department. Post recognised for final F.R.C.S. examination requirements.

JUNIOR CASUALTY OFFICER. 2 Casualty Officers employed in the Department. This is a pre-registration post.

Membership of a Medical Defence Society is a condition of appointment.

Applications, giving full details with names of 2 referees, to Group Secretary, Hospital Management Committee, St. Stephen's-road, Norwich.

NOTTINGHAM CITY HOSPITAL. (811 Beds.) Applications are invited for the post of SENIOR HOUSE OFFICER in the Department of Thoracic Surgery. Post vacant immediately. Salary £819 10s. p.a. less £150 for residential emoluments. The appointment will be for 1 year.

Applications, stating age, nationality, qualifications and experience, together with copies of 3 testimonials, should be sent to the Hospital Secretary, City Hospital, Hucknall-road, Nottingham.

NOTTINGHAM CITY HOSPITAL. (811 Beds.) Applications are invited for the post of HOUSE PHYSICIAN, vacant on 18th August, 1958. Recognised for pre-registration purposes.

Applications, stating age, nationality, qualifications and experience, together with copies of not more than 3 testimonials, to be sent immediately to the Hospital Secretary, City Hospital, Hucknall-road, Nottingham.

NOTTINGHAM GENERAL HOSPITAL. Senior House OFFICER (surgery) required. Duties to commence 26th July, 1958.

Applications, stating age, qualifications, experience and nationality, together with copies of testimonials, to be sent to Group Secretary, General Hospital, Nottingham.

NOTTINGHAM GENERAL HOSPITAL. Resident Pre-registration HOUSE PHYSICIANS required. Posts vacant July. LOCUM required immediately.

Applications, stating age, qualifications and experience, together with copies of testimonials, to be sent to Group Secretary.

NOTTINGHAM GENERAL HOSPITAL. Applications are invited for the post of SENIOR HOUSE OFFICER (casualty), duties to commence about 26th July. Establishment 3. Recognised for F.R.C.S. Post offers wide experience of casualty work.

Applications, stating age, nationality, qualifications and experience, together with copies of testimonials, to be sent to the Secretary, General Hospital, Nottingham.

NOTTINGHAM GENERAL HOSPITAL. Resident Pre-registration HOUSE SURGEONS required. Posts vacant July.

Applications, stating age, qualifications and experience, together with copies of testimonials, to be sent to Group Secretary.

OXFORD REGIONAL HOSPITAL BOARD. Registrar in Pathology (whole-time in the Swindon Area Laboratory serving a total of 1000 Beds). Post offers wide experience in all branches. The Laboratory in the new Princess Margaret Hospital, Swindon, will be opened in 1959. Post vacant 1st October, 1958. Appointment for 1 year in first instance and extension to a second year on receipt of a satisfactory report. Residential accommodation may be available.

Application forms obtainable from the Secretary, Registrars Committee, 43, Banbury-road, Oxford, should reach him by 26th July.

OLDHAM AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the resident post of HOUSE OFFICER (pædiatrics). Recognised for D.C.H. The post offers excellent neonatal experience.

Applications, containing details of qualifications and experience, together with copies of 2 recent testimonials, should be forwarded to the Group Secretary, Central Offices, Rochdale-road, Oldham.

PAISLEY HOSPITALS MATERNITY UNIT. (Thornhill AND BARSHAW MATERNITY HOSPITALS.) Applications are invited from registered and provisionally registered medical practitioners for 2 RESIDENT HOUSE SURGEON posts (obstetrics). Posts become vacant on 1st August, 1958.

Applications to Group Medical Superintendent, Royal Alexandra Infirmary, Paisley.

PAISLEY. ROYAL ALEXANDRA INFIRMARY. House SURGEON (orthopædic) required for above Infirmary as from 1st August, 1958. Post approved for pre-registration practitioners and F.R.C.S.

Applications to Group Medical Superintendent.

PAISLEY. ROYAL ALEXANDRA INFIRMARY. House SURGEONS (general) required for above Infirmary as from 1st August, 1958. Posts approved for pre-registration practitioners and F.R.C.S.

Applications to Group Medical Superintendent.

PLYMOUTH. MOUNT GOLD ORTHOPÆDIC HOS-PITAL. Applications are invited for the posts of 2 SENIOR HOUSE OFFICERS for the Orthopædic and Fracture Service, centring on Mount Gold Orthopædic and Associated Hospitals. Post recognised by R.C.S.

Applications, stating age, qualifications with dates, &c., and with copies of 2 recent testimonials, to be forwarded to the Secretary, Mount Gold Hospital, Plymouth.

PLYMOUTH. SOUTH DEVON AND EAST CORNWALL HOSPITAL.

SENIOR HOUSE OFFICER in Anæsthetics, vacant September, 1958. Recognised for the D.A. and F.F.A. R.C.S.

HOUSE SURGEONS, pre-registration posts (2) both vacant immediately. Recognised for the F.R.C.S. Greenbank Road Hospital.

In all cases send names of 3 referees, also stating age, nationality, qualifications and experience, to the Group Secretary, 7, Nelson-gardens, Stoke, Plymouth.

PLYMOUTH. SOUTH DEVON AND EAST CORNWALL HOSPITAL, FREEDOM FIELDS. Central Casualty Department. RESIDENT SENIOR HOUSE OFFICER in Casualty, vacant immediately. Recognised for the F.R.C.S.

Applications, with names of 3 referees, to be sent to the Group Secretary.

PORTSMOUTH GROUP HOSPITAL MANAGEMENT COMMITTEE. SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited for the post of ANÆSTHETIC REGISTRAR in the Portsmouth Group, with main duties at the Royal Portsmouth Hospital. Vacant 1st October, 1958. 6 Consultant Anæsthetists practise in the Group. Post recognised for F.F.A. R.C.S.

Forms of application may be obtained from the Group Secretary, Portsmouth Group Hospital Management Committee, Saint Mary's Hospital, Portsmouth, and should be returned to him, duly completed, on or before 21st July, 1958. Canvassing will disqualify. Candidates may visit the above Hospital by arrangement with the Group Secretary.

PORTSMOUTH GROUP HOSPITAL MANAGEMENT COMMITTEE.

Royal Portsmouth Hospital

Orthopædic (104 orthopædic beds)

SENIOR HOUSE OFFICER. Vacant 2nd August, 1958.

HOUSE OFFICER (pre-registration). Vacant 14th July, 1958.

Pædiatric and Medical (30 Beds)

HOUSE OFFICER (pre-registration). Vacant 12th August, 1958.

Saint Mary's Hospital

Surgery (120 surgical beds)

HOUSE OFFICERS (3) (pre-registration). Vacant now, 9th August, 1958, and 12th August, 1958.

Applications, stating age, experience and qualifications, together with the names of 2 referees, should be forwarded as soon as possible to E. H. HURST, St. Mary's Hospital, Milton-road, Portsmouth.

PRESTON ROYAL INFIRMARY. (400 Beds.) Senior SURGICAL HOUSE OFFICER. Post recognised for F.R.C.S. Vacant 1st September, 1958.

Applications, with names of 2 referees, to Group Secretary, Preston and Chorley Hospital Management Committee, Royal Infirmary, Preston.

READING. BATTLE HOSPITAL. (391 Beds.) Reading AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners for the post of RESIDENT JUNIOR HOUSE SURGEON (pre- or post-registration) required in the Accident and Orthopædic Department. F.R.C.S. recognised. Also casualty duties. Vacant immediately.

Apply, stating age, qualifications with dates, nationality, present post, with copy of recent testimonial, to Secretary.

REDHILL. EAST SURREY HOSPITAL, Shrewsbury-road, REDHILL, SURREY. RESIDENT HOUSE SURGEON (Male). Pre-registration appointment vacant immediately. Opportunity of House Physician's post to follow if required.

Applications to Hospital Secretary.

RHYL. ROYAL ALEXANDRA HOSPITAL. (138 Beds.) Applications are invited from registered medical practitioners for the post of HOUSE OFFICER in Paediatrics and General Medicine, at the above Hospital. Post tenable for 6 months.

Applications, stating age and experience, with copies of 2 testimonials, to be sent to the Group Secretary, Clwyd and Deeside Hospital Management Committee, Rhiana, Russell-road, Rhyl.

ROCHDALE GROUP OF HOSPITALS. Senior House OFFICER in Anæsthetics required. 1-year appointment recognised for the D.A. Post vacant August.

Applications to the Group Secretary, Birch Hill Hospital, Rochdale.

ROCHESTER, KENT. ST. BARTHOLOMEW'S HOSPITAL. (Recognised for the F.R.C.S.) MEDWAY AND GRAVESEND HOSPITAL MANAGEMENT COMMITTEE. HOUSE SURGEON. Applications are invited for this pre-registration post in general surgery, vacant now. Salary £467 10s.–£577 10s. p.a., according to experience.

Applications, stating age, qualifications, nationality and experience, to be addressed to the Hospital Secretary.

ROMFORD, ESSEX. RUSH GREEN HOSPITAL. Locum SURGICAL REGISTRAR required from 25th August to 7th September next for busy Surgical Unit of 120 Beds.

Apply by letter or phone to Medical Superintendent. (Tel.: Romford 46066.)

ROMFORD GROUP HOSPITAL MANAGEMENT COMMITTEE. CLINICAL ASSISTANT required on the staff of the Regional Ophthalmic Centre at Oldchurch Hospital, Romford, to undertake 1 outpatient session per week, Thursday morning, in the Eye Clinic at Tilbury and Riverside Hospital, Tilbury.

Applications to be sent to Group Secretary, Oldchurch Hospital, Romford, as soon as possible.

ROTHERHAM. MOORGATE GENERAL HOSPITAL. (342 Beds, 38 Cots.) RESIDENT HOUSE PHYSICIAN.

Applications to the Secretary, Hospital Management Committee, "Fern Bank," Doncaster-road, Rotherham.

ROTHERHAM HOSPITAL, Doncaster-gate. (161 Beds.) MOORGATE GENERAL HOSPITAL, ROTHERHAM. (342 Beds, 38 Cots.) RESIDENT HOUSE SURGEON (Casualty, E.N.T. and Eye Departments).

Applications to the Secretary, Hospital Management Committee, "Fern Bank," Doncaster-road, Rotherham.

ROTHERHAM HOSPITAL AND ROSEHILL HOSPITAL ANNEXE. (161 Beds and 26 Beds.) RESIDENT HOUSE PHYSICIAN.

Applications to the Secretary, Hospital Management Committee, "Fern Bank," Doncaster-road, Rotherham.

RUGBY. HOSPITAL OF ST. CROSS. House Surgeon in General Surgery (pre-registration). Recognised F.R.C.S. Resident.

Applications to Hospital Secretary.

RYDE. ROYAL I.W. COUNTY HOSPITAL. Isle of Wight GROUP HOSPITAL MANAGEMENT COMMITTEE. HOUSE OFFICER for pre-registration service (salary £467 10s. or £522 10s., according to experience) or SENIOR HOUSE OFFICER (salary £819 10s.) required as House Surgeon. Post recognised for F.R.C.S. Vacant August.

Applications, with names of 2 referees, to the Hospital Secretary, not later than 19th July.

SALFORD ROYAL HOSPITAL. Salford Hospital MANAGEMENT COMMITTEE. Applications invited for the undermentioned pre-registration House Officer posts which fall vacant on 21st July, 1958:—

HOUSE OFFICER (E.N.T. and neurosurgery).

HOUSE OFFICER (casualty).

Applications, with copies of 2 recent testimonials, should be sent to the Secretary, Salford Royal Hospital, Chapel-street, Salford, 3.

SCOTLAND. NORTHERN REGIONAL HOSPITAL BOARD. Applications are invited for the post of SENIOR REGISTRAR in Obstetrics and Gynæcology. The main duties are at Raigmore Hospital and the Royal Northern Infirmary, Inverness.

Schedules of application and further particulars are obtainable from the undersigned, with whom applications should be lodged by 2nd August, 1958.

A. M. FRASER, M.D.,
Secretary and Administrative Medical Officer.
Office of the Northern Regional Hospital Board,
Reay House, 17, Old Edinburgh-road, Inverness.

SHEFFIELD. CITY GENERAL HOSPITAL. (658 Beds. Recognised for F.F.A. R.C.S.) SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time RESIDENT or NON-RESIDENT REGISTRAR (anæsthetics) required immediately. The successful candidate, if non-resident, to reside at the Hospital when on call. This is a large general hospital with a department of thoracic surgery, a regional cardiological centre, and a professorial gynæcological unit. Appointment for 1 year in first instance.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 21st July, 1958, giving age, nationality, qualifications, present and previous appointments with dates, naming 3 referees.

SHEFFIELD. THE UNITED SHEFFIELD HOSPITALS. ROYAL HOSPITAL. Applications invited for the post of SENIOR HOUSE OFFICER in Neurology at the above Hospital. The candidate appointed may be required to be resident during his period of office.

Applications, stating age, qualifications and experience, with the names of 3 referees, should be sent at once to the Superintendent, Royal Hospital, West-street, Sheffield, 1.

SHOREHAM-BY-SEA, SUSSEX. SOUTHLANDS HOSPITAL. Locum REGISTRAR for Surgical and Orthopædic work required for 4 weeks from 4th August, 1958.

Apply Hospital Secretary, Southlands Hospital (phone: Shoreham by Sea 2381) as soon as possible.

A. V. OAKTON, Group Secretary,
Worthing Group Hospital Management Committee.

SHREWSBURY. EYE, EAR AND THROAT HOSPITAL. SENIOR HOUSE OFFICER (E.N.T.). Duties at E.N.T. Hospital (68 Beds) and Copthorne Hospital (168 Beds). Post recognised for the D.L.O.R.C.S. and F.R.C.S. Vacant immediately.

Applications, with copy testimonials, to the Group Secretary, Shrewsbury Hospital Group, Royal Salop Infirmary, Shrewsbury.

SHREWSBURY. ROYAL SALOP INFIRMARY/COPTHORNE HOSPITAL. (500 Beds.) HOUSE SURGEON. Vacant immediately. Pre-registration candidates eligible. Recognised for the F.R.C.S.

Applications, with copy testimonials, to Group Secretary, Shrewsbury Hospital Group, Royal Salop Infirmary, Shrewsbury.

SHREWSBURY. ROYAL SALOP INFIRMARY/COPTHORNE HOSPITAL. (500 Beds.) HOUSE PHYSICIAN, pre-registration candidates eligible. Vacant 1st August, 1958.

Applications, with copy testimonials, to Group Secretary, Shrewsbury Hospital Group, Royal Salop Infirmary, Shrewsbury.

SIDCUP, KENT. QUEEN MARY'S HOSPITAL. Resident SENIOR HOUSE OFFICER (anæsthetics) required from 15th July, 1958. Salary £819 10s., less £150 p.a. for residential emoluments. The post is recognised for the F.F.A. R.C.S. and D.A.

Applications, stating nationality, age, qualifications and experience, together with the names and addresses of 2 referees, should be sent to the Secretary.

SLOUGH, BUCKINGHAMSHIRE. UPTON HOSPITAL. Locum RESIDENT ANÆSTHETIC REGISTRAR required for 21st July–3rd August.

Applications, with names of 2 referees, to Secretary.

SOUTHAMPTON GENERAL HOSPITAL. (465 Beds.) RESIDENT HOUSE PHYSICIAN required mid-August. Pre-registration candidates eligible.

Applications, with copies of testimonials, to Group Secretary, Southampton Group Hospital Management Committee, Bullar-street, Southampton.

SOUTHAMPTON. ROYAL SOUTH HANTS HOSPITAL (274 Beds) and SOUTHAMPTON GENERAL HOSPITAL (465 Beds). SENIOR HOUSE OFFICER (E.N.T.) required end August. This post is recognised for the F.R.C.S. (Eng.) and D.L.O. examinations and provides experience in all branches of E.N.T. work. The Group includes a diagnostic and distributing hearing-aid centre.

Applications, with copies of recent testimonials, should be forwarded as soon as possible to the Secretary, Southampton Group Hospital Management Committee, Bullar-street, Southampton.

SOUTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited for an appointment as REGISTRAR in Orthopædic Surgery to the Canterbury and Isle of Thanet Groups of hospitals. A similar appointment to the Canterbury and South East Kent Groups has already been made, and duties will rotate annually between the 2 appointments, which offer experience in traumatic work and in general orthopædic surgery, including long-stay cases. The appointments will be in accordance with the terms and conditions of service of hospital medical and dental staff (England and Wales).

Applications, giving particulars of age, qualifications and experience with relevant dates, together with the names and addresses of 2 referees, to be sent to the Secretary, Registrars Committee, South East Metropolitan Regional Hospital Board, 11, Portland-place, London, W.1, not later than 26th July, 1958.

SOUTHEND-ON-SEA GENERAL HOSPITAL. Applications are invited for the post of TEMPORARY CASUALTY OFFICER (Registrar). Post vacant 18th August, 1958. Duties chiefly in Casualty Department, which is under the supervision of the Consultant in Orthopædic Surgery. Opportunities for work in fracture clinics in association with work of Orthopædic Department. The post is recognised for the F.R.C.S. if held for 6 months.

Applications, stating age, qualifications, and experience, to be sent to the Secretary by 17th July, 1958.

SOUTHEND-ON-SEA GENERAL HOSPITAL. Applications are invited for the post of RESIDENT DEPUTY CASUALTY OFFICER (Senior House Officer grade) with duties in the Fracture and Orthopædic Department, for a period of 6 months from 14th July, 1958. The post is recognised for the F.R.C.S.

Applications, stating age, qualifications and experience, with copies of recent testimonials, should reach the Secretary as soon as possible.

SOUTHEND-ON-SEA GENERAL HOSPITAL. Applications are invited for appointment as SENIOR HOUSE OFFICER to the Orthopædic and Fracture Department. Post vacant 1st August, 1958. The Orthopædic and Fracture Department is the centre for reference of all cases from a large surrounding area, and the post offers excellent experience in all aspects of orthopædic and traumatic surgery under the supervision of and with instruction from the Consultant-in-Charge. Post recognised for the F.R.C.S. Resident or non-resident.

Applications, stating age, qualifications and experience, together with copies of recent testimonials, should be sent to the undersigned by 24th July, 1958. J. C. FIELD, Secretary.

SOUTHPORT GENERAL INFIRMARY. (189 Beds. Recognised for pre-registration and F.R.C.S.) HOUSE SURGEON (general surgery and gynæcology). Post vacant July.

Apply, with 2 copy testimonials, to Group Secretary, Southport and District Hospital Management Committee, Promenade Hospital, Southport.

ST. ALBANS CITY HOSPITAL, St. Albans, Hertfordshire. (384 Beds.) Locum Tenens ANÆSTHETIC REGISTRAR, resident, required for the period 1st August–7th September, 1958, inclusive. Post recognised for F.F.A. R.C.S. and D.A.

Applications to Secretary, Mid Herts Group Hospital Management Committee, Bleak House, Catherine-street, St. Albans.

ST. ALBANS CITY HOSPITAL. (384 Beds.) North WEST METROPOLITAN REGIONAL HOSPITAL BOARD. Whole-time SURGICAL REGISTRAR required for duties in General Surgical and Orthopædic Departments. Post vacant about 21st September, 1958. Hospital may be visited by direct appointment.

Application forms obtainable from, and returnable to, Secretary, Mid-Herts Group Hospital Management Committee, Bleak House, Catherine-street, St. Albans, Herts, by 22nd July, 1958.

ST. ALBANS CITY HOSPITAL. (384 Beds.) North West METROPOLITAN REGIONAL HOSPITAL BOARD. Whole-time ANÆSTHETIC REGISTRAR required. Post recognised for F.F.A.R.C.S. and D.A., and vacant about 27th August, 1958. Hospital may be visited by direct appointment.

Application forms obtainable from and returnable to Secretary, Mid Herts Group Hospital Management Committee, Bleak House, Catherine-street, St. Albans, Herts.

ST. ALBANS CITY HOSPITAL. (384 Beds.) North West METROPOLITAN REGIONAL HOSPITAL BOARD. CASUALTY OFFICER (Registrar grade) required. Post recognised for F.R.C.S. regulations. Appointment tenable for 6 months from 1st September, 1958, and subject to review at end of this period.

Application forms obtainable from and returnable to Secretary, Mid-Herts Group Hospital Management Committee, Bleak House, Catherine-street, St. Albans, Herts.

ST. ASAPH HOSPITAL, St. Asaph, Flintshire. Appointment of HOUSE OFFICER. Duties divided between ophthalmology (16 Beds), E.N.T. (12 Beds), and oral surgery (4 Beds).

Applications, stating age, qualifications and experience, accompanied by 2 recent testimonials, to be sent forthwith to the Group Secretary, Clwyd and Deeside Hospital Management Committee, Rhianfa, Russell-road, Rhyl.

STAFFORD. STAFFORDSHIRE GENERAL INFIRMARY. (175 Beds—Recovery Unit 32 Beds.) HOUSE SURGEON. Pre-registration post. Vacant 9th July. At end of service the successful applicant will be considered for appointment to a pre-registration post of House Physician if he or she has not held such an appointment.

Applications to Group Secretary, Stafford Hospital Management Committee, 13, Foregate-street, Stafford.

STOCKPORT AND BUXTON HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of SENIOR HOUSE OFFICER (anæsthetics) with duties at Stepping Hill Hospital, Stockport (529 Beds) and Stockport Infirmary (163 Beds). The post is recognised for the D.A. and F.F.A. R.C.S., and there are ample opportunities for study.

Applications, stating age, experience and qualifications, together with copies of 2 testimonials, to be addressed to the Secretary, Stockport and Buxton Hospital Management Committee, 59B, Shaw-heath, Stockport.

STOCKPORT INFIRMARY. (163 Beds.) Locum Senior HOUSE OFFICER (medicine) required.

Applications, with copies of 2 testimonials, to the Secretary, Stockport and Buxton Hospital Management Committee, 59B, Shaw-heath, Stockport.

STOCKPORT. STEPPING HILL HOSPITAL. (529 Beds.) Applications are invited for the post of HOUSE OFFICER (general surgery).

Applications, with copies of 2 testimonials, to the Group Secretary, Stockport and Buxton Hospital Management Committee, 59B, Shaw-heath, Stockport.

STOCKPORT. STEPPING HILL HOSPITAL. (529 Beds.) Applications are invited for 2 pre-registration posts of HOUSE OFFICER (medicine), vacant 31st July, 1958, and 21st August, 1958.

Applications, with full particulars and copies of 2 testimonials, to the Secretary, Stockport and Buxton Hospital Management Committee, 59B, Shaw Heath, Stockport.

STOKE-ON-TRENT. NORTH STAFFORDSHIRE ROYAL INFIRMARY. SENIOR HOUSE OFFICER (anæsthetics) required. Post recognised for F.F.A. R.C.S. and D.A. Medical library facilities available.

Detailed applications to Hospital Secretary as soon as possible.

STOKE-ON-TRENT. NORTH STAFFORDSHIRE ROYAL INFIRMARY. HOUSE OFFICER (general surgery) required. Recognised for F.R.C.S. Post vacant very shortly.

Detailed applications, with copy testimonials, to Hospital Secretary, North Staffordshire Royal Infirmary, Stoke-on-Trent.

SULLY HOSPITAL, Sully, Glamorganshire. (Thoracic centre of 324 Beds.) SENIOR HOUSE OFFICER (surgical)—applicants primarily interested in general surgery considered. Experience will be gained in investigation and treatment of chest and heart conditions.

Form of application from Group Secretary, 44, Cathedral-road, Cardiff.

SUTTON AND CHEAM HOSPITAL, Cotswold-road, SUTTON, SURREY. (146 Beds.) HOUSE PHYSICIAN (post approved for pre-registration). Post vacant 1st August.

Applications, stating age, experience and qualifications, with copies of recent testimonials and the names of 2 referees, to the Secretary at above address.

SWANSEA. MORRISTON HOSPITAL. Glantawe HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of SENIOR HOUSE OFFICER in the Department of Neurosurgery at the above Hospital. The Department is the centre for neurosurgery for South West Wales, and the post offers facilities for the study of neurology for those studying for higher qualifications. Vacancy 1st August, 1958.

Applications, together with copies of 2 recent testimonials, should be forwarded to the Medical Superintendent of the Hospital. T. E. JONES, Group Secretary.

SWINDON AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for post of RESIDENT HOUSE PHYSICIAN in acute medical unit of 64 Beds at St. Margaret's Hospital. Recognised for training under pre-registration internship regulations.

Full details, with names of 3 referees, to Secretary, 7, Okus-road, Swindon.

TAUNTON AND SOMERSET HOSPITAL, Taunton, SOMERSET. (423 Beds.) HOUSE OFFICER (general surgery) required. Pre-registration post recognised for F.R.C.S., vacant now.

Applications, stating age, nationality and qualifications, to the Group Secretary, Taunton Hospital Management Committee, c/o Musgrove Park Hospital, Taunton.

TAUNTON AND SOMERSET HOSPITAL. Applications are invited for the post of SENIOR HOUSE OFFICER (casualty and orthopædic).

Applications, stating age, nationality and qualifications, together with the names of 2 referees, should be forwarded to the Group Secretary, Taunton Hospital Management Committee, Taunton and Somerset Hospital, Musgrove Park Branch, Taunton, Somerset.

TAPLOW, near MAIDENHEAD. CANADIAN RED CROSS MEMORIAL HOSPITAL. HOUSE PHYSICIAN required for post vacant 26th August. Pre-registration post.

Applications, stating age, experience and qualifications with dates, and copies of 2 testimonials, to Secretary.

TORQUAY. TORBAY HOSPITAL. Resident Casualty OFFICER (Senior House Officer status) required August, 1958. Post recognised for F.R.C.S. purposes. There is a complement of 6 Resident House Officers.

Applications, stating qualifications, nationality, age, (quoting Ref. F. 955/86) with copy testimonials, to the Group Secretary, Torquay District Hospital Management Committee, Torbay Hospital, Torquay, S. Devon.

WAKEFIELD. PINDERFIELDS GENERAL HOSPITAL. (Regional Thoracic Centre.) Applications invited for positions of SENIOR HOUSE PHYSICIAN and SENIOR HOUSE SURGEON. Salary £819 10s. p.a. £150 p.a. charged for accommodation.

Address written applications, giving full personal particulars, details of experience and 2 names and addresses for reference, to W. BOWRING, Group Secretary, Pinderfields General Hospital, Wakefield.

WAKEFIELD. PINDERFIELDS GENERAL HOSPITAL. Locum Tenens SENIOR HOUSE PHYSICIAN required for the period 17th–31st July, inclusive. Salary £15 19s. per week. Charge for accommodation at the rate of £150 p.a.

Address written applications, giving full personal particulars, details of experience and 2 names and addresses for reference, to W. BOWRING, Group Secretary, Pinderfields General Hospital, Wakefield.

WAKEFIELD. PINDERFIELDS GENERAL HOSPITAL. Applications invited for position of SENIOR HOUSE OFFICER in the Neurological Department. Salary £819 10s. p.a. A charge of £150 p.a. is made for accommodation.

Address written applications, giving full personal particulars and details of experience, &c., together with 2 names and addresses for reference, to W. BOWRING, Group Secretary, Pinderfields General Hospital, Wakefield.

WAKEFIELD. STANLEY ROYD HOSPITAL. Applications invited for post of JUNIOR HOSPITAL MEDICAL OFFICER or SENIOR HOUSE OFFICER in Psychiatry. Accommodation available for a single person.

Address written applications, giving full personal particulars, details of training, experience, &c., and 2 names and addresses for reference, to W. BOWRING, Group Secretary, Pinderfields General Hospital, Wakefield.

WALSALL HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the following appointments:—

Manor Hospital (340 Beds)
HOUSE PHYSICIAN.
General (Sister Dora) Hospital (181 Beds)
HOUSE PHYSICIAN.
Recognised for pre-registration.

Applications, together with names of 2 referees, to Group Secretary, Walsall General (Sister Dora) Hospital.

WALSALL HOSPITAL MANAGEMENT COMMITTEE.
Manor Hospital, Walsall
PÆDIATRIC HOUSE PHYSICIAN required 1st August, 1958; recognised for D.C.H., also pre-registration.

Applications, together with names of 2 referees, to Group Secretary, Walsall General (Sister Dora) Hospital.

WALSALL HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the following appointments:—

Manor Hospital (340 Beds)
HOUSE SURGEON.
General (Sister Dora) Hospital (181 Beds)
HOUSE SURGEON.
Recognised for pre-registration.

Applications, together with names of 2 referees, to Group Secretary, Walsall General (Sister Dora) Hospital.

WARRINGTON AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the resident post of SENIOR HOUSE OFFICER (geriatrics) (Male or Female) for active geriatric units at Whitecross Hospital and Aikin Street Hospital, Warrington. Good clinical experience and study time for higher qualifications. Scale of salary £819 10s. p.a., less a deduction of £150 p.a. for residential emoluments.

Applications to be forwarded to HENRY L. BOOT, Group Secretary, c/o General Hospital, Warrington, Lancs.

WARRINGTON INFIRMARY. Applications are invited from Males and Females for the post of RESIDENT CASUALTY OFFICER (graded as Junior Hospital Medical Officer) at the above Hospital. The post is recognised for the F.R.C.S. Scale of salary £852 10s.–£55–£1182 10s. less a deduction of £170 for residential emoluments. A whole-time Senior Hospital Medical Officer is in charge of the Department.

Applications, stating age, experience and qualifications, should be forwarded to—

HENRY L. BOOT, Group Secretary,
Warrington and District Hospital Management Committee,
c/o General Hospital, Warrington, Lancs.

WEST CUMBERLAND HOSPITAL MANAGEMENT COMMITTEE. JUNIOR HOSPITAL MEDICAL OFFICER in Anæsthetics required for work throughout the West Cumberland Group but based on Whitehaven Hospital. Good experience essential, and possession of the D.A. preferred.

Apply, with full information as to qualifications and experience, and giving the names of 2 referees, to the Group Secretary at Workington Infirmary.

WATFORD, HERTFORDSHIRE. PEACE MEMORIAL HOSPITAL. (211 Beds.) Applications are invited for the post of HOUSE SURGEON at the above Hospital. This is a pre-registration post and is recognised for F.R.C.S. Salary according to the National Health Service scale. Post vacant mid-July.

Please send copies of recent testimonials, with applications, to the Administrator.

WATFORD, HERTFORDSHIRE. PEACE MEMORIAL HOSPITAL. (211 Beds.) Applications are invited for the post of RESIDENT ANÆSTHETIST (Senior House Officer grade) to the Watford Hospitals. Post vacant 1st July.

Applications, together with copies of not more than 2 recent testimonials, to the Administrator.

WATFORD HOSPITALS. North West Metropolitan REGIONAL HOSPITAL BOARD. ANÆSTHETIC REGISTRAR (resident) required for the above Hospitals. Application made for recognition. Post vacant mid-August.

Application forms obtainable from and returnable to Secretary, West Herts Group Hospital Management Committee, 9, Rickmansworth-road, Watford, Herts, by 15th July, 1958.

WATFORD. SHRODELLS HOSPITAL. (General hospital, 366 Beds.) Applications are invited for the post of SENIOR HOUSE OFFICER to the Geriatric Unit. Resident or non-resident, to take up duty about July 25th. This unit of 180 Beds, under a full-time Consultant Geriatrician, offers excellent clinical experience in diagnosis and treatment of acute and other illnesses in the elderly. Full laboratory and radiological facilities. Adequate time for reading.

Applications, together with copies of not more than 2 testimonials, should reach the Medical Administrator as soon as possible.

WELSH REGIONAL HOSPITAL BOARD.

REGISTRAR in Anæsthetics, Maelor General Hospital, Wrexham (591 Beds).

REGISTRAR in Thoracic Medicine, Llangwyfan Hospital, near Denbigh. Modern methods of treatment tuberculosis and chest diseases. 370 adult beds (Male and Female) and children. Hospital also contains major thoracic unit. Vacant 7th September, 1958.

REGISTRAR (general surgery), Royal Alexandra Hospital, Rhyl (138 Beds). Vacant 6th October, 1958.

Subject to review end of first year.

Application forms from Senior Administrative Medical Officer, Temple of Peace, Cathays Park, Cardiff, within 10 days.

WEST BROMWICH AND DISTRICT HOSPITALS MANAGEMENT COMMITTEE. Applications are invited for the following appointments. Pre-registration.

West Bromwich and District General Hospital (144 Beds)

1 HOUSE PHYSICIAN.

Hallam Hospital, West Bromwich (430 Beds)

2 HOUSE PHYSICIANS.

These posts will be vacant 8th July, 1958.

Applications, with 3 recent testimonials, to Group Secretary, West Bromwich and District Hospital Management Committee, Edward-street, West Bromwich.

WESTON-SUPER-MARE GENERAL HOSPITAL. (104 Beds.) Applications are invited from duly qualified medical practitioners for the pre-registration appointment of HOUSE SURGEON (resident). Vacancy 15th July, 1958.

Applications, stating age, qualifications, together with names and addresses of 2 referees, should be addressed to the Secretary, Weston-super-Mare Hospital Management Committee.

WIGAN AND LEIGH HOSPITAL MANAGEMENT COMMITTEE. ASTLEY HOSPITAL, ASTLEY, NEAR MANCHESTER. SENIOR HOUSE OFFICER in Surgery required. Duties include gynæcology and casualty. Resident post. Vacant now.

Apply Secretary, Knowsley House, Wigan.

WINDSOR. KING EDWARD VII HOSPITAL. Registrar (Casualty Officer), resident, required. There is an Accident Unit of 30 Beds at the Hospital and with the Casualty Department forms part of the Accident Service for the Windsor Group and includes duties with the E.N.T. and Eye Departments. Candidates should have had previous experience in the treatment of acute injuries.

Application forms from and returnable to Secretary, Windsor Group Hospital Management Committee, Alma-road, Windsor.

WOLVERHAMPTON. NEW CROSS HOSPITAL. (634 Beds.) 1 SENIOR HOUSE OFFICER and 2 HOUSE OFFICERS (pre-registration), Medicine. Acute medical beds. Vacant now.

Applications to Hospital Secretary.

WOLVERHAMPTON. THE ROYAL HOSPITAL. (An associated hospital of the Birmingham University Medical School.) Pre-registration HOUSE OFFICER (general surgery). Post vacant immediately. Recognised for F.R.C.S.

Apply, giving age and qualifications and copies of 2 testimonials, to the Secretary.

WOLVERHAMPTON. THE ROYAL HOSPITAL. (An associated hospital of the Birmingham University Medical School.) Pre-registration HOUSE OFFICER (pædiatrics). Post recognised for D.C.H. Vacant immediately.

Apply, giving age and qualifications and copies of 2 testimonials, to the Secretary.

WORCESTER ROYAL INFIRMARY. (213 Beds.) Locum Tenens HOUSE PHYSICIAN required from 27th July to 10th August.

Applications to Hospital Secretary.

WORKSOP. VICTORIA HOSPITAL. (119 Beds—28 orthopædic beds. Recognised for F.R.C.S.) SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time REGISTRAR (orthopædics and casualty) required immediately. Furnished married accommodation available. Appointment for 1 year in first instance.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 21st July, 1958, giving age, nationality, qualifications, present and previous appointments with dates, naming 3 referees.

WORTHING HOSPITAL, Lyndhurst-road, Worthing, SUSSEX. (210 Beds. Acute general.) The post of HOUSE PHYSICIAN will be vacant 31st August.

Applications from fully registered medical practitioners, stating age, qualifications, experience, nationality and enclosing copies of 2 recent testimonials, to be forwarded to the Hospital Secretary immediately.

A. V. OAKTON, Group Secretary,
Worthing Group Hospital Management Committee.

WORTHING HOSPITAL, Lyndhurst-road, Worthing, SUSSEX. (210 Beds. Acute general.) The post of HOUSE SURGEON will be vacant from 10th August.

Applications from either registered medical practitioners or pre-registration candidates, stating age, qualifications, experience, nationality and enclosing copies of 2 recent testimonials to be forwarded to the Group Secretary immediately.

A. V. OAKTON, Group Secretary,
Worthing Group Hospital Management Committee.

WREXHAM. MAELOR GENERAL HOSPITAL (591 Beds) and WAR MEMORIAL HOSPITAL, WREXHAM (230 Beds). Applications are invited for HOUSE SURGEON posts at the above Hospitals, duties to commence on 1st August, 1958. The appointments are recognised for the Diploma of F.R.C.S. (England, Edinburgh and Ireland) and are pre-registration posts.

Applications, stating age, nationality, qualifications, and experience, with copies of 2 recent testimonials, to be sent to the Group Secretary, Wrexham, Powys and Mawddach Hospital Management Committee, Maelor General Hospital, Wrexham, as soon as possible.

WREXHAM. MAELOR GENERAL HOSPITAL. (591 Beds.) Applications are invited for the post of PÆDIATRIC HOUSE PHYSICIAN at the above Hospital, to commence 1st August, 1958. The appointment is recognised for the D.C.H. and for pre-registration purposes.

Applications, stating age, nationality, qualifications and experience, together with copies of 2 recent testimonials, should be addressed to the Group Secretary, Wrexham, Powys and Mawddach Hospital Management Committee, Maelor General Hospital, Wrexham, Denbighshire.

WREXHAM. MAELOR GENERAL HOSPITAL (591 Beds) and WAR MEMORIAL HOSPITAL, WREXHAM (230 Beds). Applications are invited for HOUSE PHYSICIAN posts at the above Hospitals, to commence 1st August, 1958. The appointments are recognised for pre-registration purposes.

Applications, stating age, nationality, qualifications and experience, together with copies of 2 recent testimonials, should be addressed to the Group Secretary, Wrexham, Powys and Mawddach Hospital Management Committee, Maelor General Hospital, Wrexham, Denbighshire.

WREXHAM (near). TREVALYN MANOR MATERNITY HOSPITAL, ROSSETT, near WREXHAM. (47 Beds.) Applications are invited for the post of HOUSE SURGEON at the above Hospital, to commence duties on 1st September, 1958. The Hospital is a Part II Midwifery Training School and deals with normal and abnormal midwifery.

Applications, stating age, nationality, qualifications and experience, with copies of 2 recent testimonials, to be sent to the Group Secretary, Maelor General Hospital, Wrexham, as soon as possible.

WREXHAM. WAR MEMORIAL HOSPITAL. (230 Beds.) Applications are invited for the post of SENIOR HOUSE OFFICER in the Orthopædic Department of the above Hospital. The post is a residential one and affords particular facilities for postgraduate study. Successful applicant will be allowed to attend for 2 days a month at the Robert Jones and Agnes Hunt Orthopædic Hospital, Oswestry. The Hospital is recognised for the Diploma of F.R.C.S. (England, Edinburgh, and Ireland).

Applications, stating age, nationality, qualifications, and experience, together with copies of 2 recent testimonials, to be addressed to the Group Secretary, Maelor General Hospital, Wrexham, as soon as possible.

CANADA. REGINA GENERAL HOSPITAL, Regina, SASKATCHEWAN. The following vacancies exist for appointments in an 800-Bed hospital, all services very active:—

(1) JUNIOR ROTATING INTERNSHIPS, stipend $150 per month, plus full maintenance.

(2) ASSISTANT-RESIDENTS in Pathology, stipend $200 per month, plus full maintenance.

(3) ASSISTANT-RESIDENTS and RESIDENTS in Surgery, stipend at the rate of $200 per month for Assistant-Residents and $250 per month for Residents, plus full maintenance.

Apply: Superintendent, Regina General Hospital, Regina, Saskatchewan, Canada.

NEW YORK. NEW ROCHELLE HOSPITAL, New ROCHELLE, NEW YORK, U.S.A. (383-Bed general community hospital.) Approved by the Joint Commission on Accreditation of Hospitals. Also approved by the American College of Surgeons and American Medical Association for Internship and Residency training. Only graduates from approved university schools accepted. Internships available for the 1-year term commencing 1st July, 1958. Stipend is $200 per month plus complete maintenance.

Apply Superintendent.

ST. JOHN'S, NEWFOUNDLAND, CANADA. GENERAL HOSPITAL. (456 Beds.) The above Hospital has vacancies for INTERNES, for which applications are invited, salary $2500 p.a., less $528 for maintenance. There is a full teaching programme, the Hospital is fully approved by the Canadian Medical Association for Interne training, approved by the Royal College of Physicians and Surgeons in Canada for postgraduate training towards certification and also recognised under the United Kingdom Medical Act for pre-registration year. Transport to St. John's will be provided and on completion of 1 year's service, return fare to the United Kingdom will be provided.

Applications, with full details as to age, &c., together with names of 2 referees, should be forwarded immediately to Dr. E. WILSON, Superintendent, General Hospital, St. John's, Newfoundland, Canada.

IBADAN, NIGERIA. UNIVERSITY COLLEGE HOSPITAL. For SENIOR HOUSE OFFICERS/REGISTRARS posts, please see under Hospital Services: Senior Appointments, page 53.

Public Appointments

BIRMINGHAM. CITY OF BIRMINGHAM. Public HEALTH DEPARTMENT. Applications are invited for the appointment of ASSISTANT MEDICAL OFFICER (Male or Female) for Maternity and Child Welfare. The duties will be mainly in connection with Maternity and Child Welfare as well as the medical aspects of the care of deprived children in the care of the Children's Department. Salary scale £1050–£50 (3)–£55 (5)–£1475 p.a. with placement on the scale according to qualification and experience. Pension scheme (including widows and orphans); medical examination.

Applications, giving full particulars of qualifications and experience, together with names of 3 persons to whom reference may be made, to be sent to Medical Officer of Health, Council House, Birmingham, 3, not later than 26th July, 1958.

GLOUCESTERSHIRE COUNTY COUNCIL. Assistant COUNTY MEDICAL OFFICER OF HEALTH AND SCHOOL MEDICAL OFFICER (Male). Must be registered medical practitioner. Possession of a Diploma or Certificate in Public Health an advantage. Salary £1050–£1475 p.a. Superannuable. Medical examination. Car driver and should possess a motorcar.

Application forms obtainable from County Medical Officer of Health, Berkeley House, Berkeley-street, Gloucester, returnable by 2nd August, 1958.

GUY H. DAVIS, Clerk of the County Council.

Shire Hall, Gloucester.

LANCASHIRE COUNTY COUNCIL. Applications are invited from registered medical practitioners for appointment as ASSISTANT DIVISIONAL MEDICAL OFFICER in the Liverpool area. Possession of Diploma in Public Health desirable. Salary £1050 rising to £1475 p.a. Travelling and subsistence allowances where applicable.

Application forms and further particulars from County Medical Officer, Serial 923, East Cliff County Offices, Preston. Application forms to be returned by 31st July, 1958.

MONMOUTHSHIRE COUNTY COUNCIL. The Council invite applications from duly qualified registered medical practitioners for the appointment of ASSISTANT MEDICAL OFFICER to the Refraction Unit. Preference will be given to applicants with experience in refraction work. The salary will be at the rate of £1050 p.a., rising by annual increments of £50 to £1200 and then by £55 to a maximum of £1475. The successful candidate will be required to act under the direction of the County Medical Officer, to devote his her whole time to the work of the County Council and to reside in such place as the County Council may determine. The post will be subject to the provisions of the Local Government Superannuation Acts and Regulations and to a satisfactory medical examination.

Application forms and conditions of service can be obtained from the County Medical Officer, Cambria House, Caerleon, to whom they should be returned, accompanied by copies of not more than 3 testimonials, not later than 14th July, 1958.

VERNON LAWRENCE, Clerk of the Council.

County Hall, Newport, Mon.

STAFFORDSHIRE COUNTY COUNCIL. Health Department. Appointment of COUNTY PSYCHIATRIST. Applications are invited from registered medical practitioners with suitable experience to undertake duties involving the day-to-day control of the Mental Health Section of the Department, including Mental Deficiency and Lunacy, together with Child Guidance arrangements of the School Health Service. Practical experience of child guidance work is desirable and the possession of a Diploma in Psychological Medicine will be considered an advantage. The candidate will be on the staff of the County Medical Officer of Health, to whom he will be responsible. The salary scale will be in accordance with the latest Industrial Court Award, i.e., £1520 p.a., rising by annual increments of £50 (1) and £55 (7) to £1955 p.a., and previous similar service may be taken into consideration when deciding the commencing rate. The candidate appointed will be required to provide a car and will be paid allowances in accordance with the County Council's scale. The appointment, which will be terminable by 3 months' notice in writing on either side, will also be subject to the provisions of the appropriate superannuation Acts and regulations, in which connection the successful candidate will be required to pass a medical examination and produce his or her birth certificate.

Applications, stating age, qualifications and experience, together with copies of not more than 3 recent testimonials, should reach the County Medical Officer of Health, County Buildings, Stafford, not later than 31st July, 1958. Canvassing, directly or indirectly, will disqualify, and all applicants must state whether, to their knowledge, they are related to any member or senior officer of the County Council.

T. H. EVANS, Clerk of the County Council.

County Buildings, Stafford. 2nd July, 1958.

THE MEDICAL SERVICE OF THE ROYAL NAVY

VACANCIES FOR MEDICAL OFFICERS

Candidates are invited for Short Service Commissions of 3 years, on termination of which a gratuity of £600 (tax free) is payable. Ample opportunity is granted for transfer to Permanent Commissions on completion of 1 year's total service. Officers so transferred are paid instead a grant of £1500 (taxable).

All entrants are required to be British subjects whose parents are British subjects, medically qualified, physically fit, and to pass an interview.

Full particulars from the Admiralty Medical Department, Queen Anne's Mansions, St. James's Park, London, S.W.1.

FACTORY DOCTORS. Factories Acts, 1937 and 1948. The following appointments as Appointed Factory Doctor are vacant. Apply to Chief Inspector of Factories, 19, St. James's-square, London, S.W.1.

District	*County*	*Latest date for receipt of applications*
MERE	.. WILTSHIRE ..	.. 26TH JULY, 1958
CHATHAM ..	.. KENT	.. 26TH JULY, 1958

LINDSEY COUNTY COUNCIL. Health Department. Applications invited from fully qualified medical Women for post of ASSISTANT MEDICAL OFFICER for Maternity and Child Welfare for Cleethorpes area of Lindsey. Whitley Council salary, i.e., £1050 p.a. rising by 3 annual increments of £50 and 5 annual increments of £55 to maximum of £1475 p.a.

Further particulars and application forms obtainable from DR. C. D. CORMAC, County Health Department, County Offices, Lincoln. Closing date for receipt of applications 28th July, 1958.

NORTHAMPTON COUNTY BOROUGH. Assistant MEDICAL OFFICER OF HEALTH AND SCHOOL MEDICAL OFFICER. (£1050–£50–£1200–£55–£1475.)

Particulars and form of application, returnable by 21st July, from Medical Officer of Health, 7A, St. Giles'-square, Northampton. C. E. VIVIAN ROWE, Town Clerk.

SALFORD. CITY OF SALFORD. Health Department. SENIOR ASSISTANT MEDICAL OFFICER. Applications for this post are invited from qualified medical practitioners preferably with the D.C.H. or D.P.H. qualification. The appointment will be permanent and whole-time and the salary will be in accordance with the scale—£1465, rising by £55 annually to £1795 p.a. The commencing salary will be fixed within the scale according to qualifications and experience. The post is superannuable.

Form of application and other particulars relating to the appointment may be obtained from the Medical Officer of Health, 143, Regent-road, Salford, 5, by whom applications (including names of 2 referees) must be received not later than 19th July, 1958. R. RIBBLESDALE THORNTON, Town Clerk.

SURREY COUNTY COUNCIL. Mixed Appointment of SURREY COUNTY DIVISIONAL MEDICAL OFFICER, MEDICAL OFFICER OF HEALTH for Coulsdon and Purley and Caterham and Warlingham (separate appointments). Applications invited from fully-qualified registered medical practitioners for these appointments, superannuable and subject to medical examination and Sanitary Officers (Outside London) Regulations, 1935–51. Salary within scale £2012 19s. 1d. to £2380 2s. 3d. according to experience.

Applications, giving age, qualifications, experience and names of 3 referees, to County Clerk, County Hall, Kingston-upon-Thames, by 25th July, 1958. Canvassing disqualifies.

W. W. RUFF,
Clerk of Surrey County Council.

ERIC F. J. FELIX,
Clerk of Coulsdon and Purley Urban District Council.

B. J. SMERDON,
Clerk of Caterham and Warlingham Urban District Council.

YORKSHIRE. COUNTY COUNCIL OF THE WEST RIDING OF YORKSHIRE. Appointment of County Medical Officer of Health. The County Council of the West Riding of Yorkshire invite applications for the appointment of MEDICAL OFFICER OF HEALTH AND PRINCIPAL SCHOOL MEDICAL OFFICER for the County. The salary will be £3285 p.a., rising by 3 annual increments of £105 and 1 of £55 to £3655 p.a. Candidates must not only be duly qualified as prescribed by the Local Government Act, 1933, but must also possess considerable administrative ability and a wide knowledge and experience of the organisation of public health services.

The prescribed form of application with terms and conditions of the appointment may be obtained from the undersigned. Applications on the form provided, together with copies of not more than 3 recent testimonials, should be sent marked "Confidential", not later than 30th September, 1958, addressed to the Clerk of the County Council, County Hall, Wakefield. Canvassing, directly or indirectly, will be a disqualification.

BERNARD KENYON, Clerk of the County Council.

County Hall, Wakefield. July, 1958.

YORKSHIRE. COUNTY COUNCIL OF THE WEST RIDING OF YORKSHIRE. Appointment of ASSISTANT COUNTY MEDICAL OFFICER AND SCHOOL MEDICAL OFFICER, Horsforth (near Leeds) Division. Applications invited from registered medical practitioners with at least 3 years' experience since qualification. Duties mainly in School Health and Infant Welfare Services. Salary £1050–£1475 p.a. County Council scale of travelling and subsistence allowances. Post superannuable and subject to medical examination.

Forms of application from the undersigned to be returned not later than 26th July, 1958.

J. LEIPER, Deputy County Medical Officer.

County Hall, Wakefield.

GOVERNMENT OF LEEWARD ISLANDS. Applications invited from doctors with qualifications registrable in United Kingdom for following posts. F.R.C.S. required for (*a*).

(*a*) MEDICAL SUPERINTENDENT to superintend and administer Cunningham Hospital, St. Kitts, and to be responsible for treatment and care of all inpatients. Appointment on permanent basis with pension (non-contributory). Salary £1380 p.a. Travelling allowance of £100 p.a. also payable. Certain operation and consultation fees, as laid down in local regulations.

(*b*) DISTRICT MEDICAL OFFICER to give treatment at dispensaries and health clinics, serve as health officer for post health work and quarantine, carry out preventive inoculations and supervise all health work in his district. Salary scale £720–£900 p.a. Private practice permitted.

Appointment on agreement for approximately 2 years in first instance. Free unfurnished quarters provided. Free passages for officer, wife, and not more than 3 unmarried dependent children under 18 years. Generous leave.

Application forms from Director of Recruitment, Colonial Office, S.W.1 (quoting BCD.117/33/013).

GALWAY. WESTERN HEALTH INSTITUTIONS BOARD. Applications are invited from suitable candidates for appointment to the office of Whole-time TEMPORARY SURGICAL REGISTRAR under the Western Health Institutions Board.

Remuneration: £800–£100–£1000 a year plus £100 a year in the case of a person having a higher surgical qualification, plus temporary bonus (at present £62 10s. on £800 to £82 on £1100), subject to an appropriate deduction in respect of emoluments provided in kind.

Age-limit: 24–40 years on 1st March, 1958.

Qualifications: At least 3 years' experience, including 2 years' satisfactory surgical experience. Previous experience in thoracic surgery is desirable.

Application forms and further particulars may be had on application to the Secretary, Western Health Institutions Board, Merlin Park, Galway. Latest date for the reception of completed applications, Tuesday, 22nd July, 1958.

GHANA PUBLIC SERVICE COMMISSION. Applications are invited for the following vacancies in the Ministry of Health:

SPECIALIST RADIOLOGIST. To carry out radiological diagnosis at the main hospital and organise and control the X-ray services in Ghana. Must be registered medical practitioner and possess D.M.R.D. or D.M.R.E. with 4 years' approved full-time hospital experience in general radiological work. Salary according to qualifications and experience in range £2400–£2700 a year.

RADIOLOGIST. To take charge of X-ray Department, carry out diagnosis of treatment and train Junior Staff. Must be registered medical practitioner and possess D.M.R.D. or D.M.R.E. or similar qualification. Salary according to qualification and experience in range £1380–£2400 p.a.

MEDICAL OFFICERS OF HEALTH. To prevent disease and carry out treatment whenever necessary. Must be registered medical practitioners and possess Diploma of Public Health or similar recognised qualification. Salary according to qualification and experience in range £1380–£2400 p.a.

Appointments are on contract for 2 tours each of 18–24 months duration. Gratuity at rate of £12 10s. for each completed month of residential service payable on completion of contract. Outfit allowance £30–£60 on first appointment. Free first-class passages for Officer, wife and up to 3 children under 18 years and in addition an education allowance for children when not resident in Ghana of £100 a child for up to 3 children under 18 years. Generous home leave on full pay. Income-tax at low local rates. Preservation of superannuation or pension rights, where applicable, can be arranged.

For further particulars and application form write, stating age, qualifications and experience, to the Director of Recruitment, Ghana High Commissioner's Office, 13, Belgrave-square, London, S.W.1.

General Practice

For an ***Executive Council post*** *(England and Wales) apply on form E.C.16A obtainable from the council. Mark envelope "Vacancy."*

TOTTENHAM. Applications invited for Vacancy occasioned by resignation of practitioner. List at present approximately 2600. "Restricted" area. Premises will not be available. Apply on Form E.C.16A before 19th July, 1958, to The Clerk, Middlesex Executive Council, North West House, 119-127, Marylebone-road, London, N.W.1.

HARLECH, NORTH WALES. Applications invited for VACANCY (Rural). List approximately 1885. Knowledge of Welsh desirable. Accommodation available for purchase or rental. Apply on Form E.C.16A by 24th July, 1958.

Beechwood House, Dolgellau. D. G. ROBERTS, Clerk, Merioneth Executive Council.

CORRIS, near MACHYNLLETH, NORTH WALES. Applications invited for VACANCY (Rural). List approximately 975. Knowledge of Welsh desirable. An inducement payment was made to the previous doctor, and the Council will recommend payment to a suitable doctor. Apply on Form E.C.16A by 24th July, 1958.

Beechwood House, Dolgellau. D. G. ROBERTS, Clerk, Merioneth Executive Council.

ROMILEY, CHESHIRE. Applications are invited for a VACANCY, due to retirement. Duties to commence 1st October, 1958. Urban area. List at present approximately 1500. House and surgery available for purchase. Applications on Form E.C.16A to be submitted not later than 23rd July, 1958, to the Clerk of the Cheshire Executive Council, 28, Nicholas-street, Chester.

TUNBRIDGE WELLS, KENT. Applications invited for VACANCY (Urban). List at present approximately 1250. Residence and surgery not likely to be available. Apply on E.C.16A before 26th July, 1958, to—

F. E. MILES, Clerk,
Kent and Canterbury Executive Council.
11, Station-road, Maidstone.

Hospital Services: Non-Medical Appointments

BEVERLEY, EAST YORKSHIRE. WESTWOOD HOSPITAL. BIOCHEMIST, non-medical, basic grade, for Area Laboratory; Whitley scale.

Applications, with details of age, qualifications and experience, and names of 2 referees, to Hospital Secretary.

Miscellaneous

Translator required for translating German literature on ethical pharmaceutical specialties into English. Applicants with medical background and with experience in this kind of work willing to reside permanently in Western Berlin (Federal Republic of Germany) are requested to forward their application with curriculum vitæ and photo, stating salary expected, to SCHERING A.G., Berlin, N.65, Muellerstrasse 170–172.

The Medical Defence Union. Applications are invited from registered medical practitioners, not exceeding 35 years of age, for appointment as an Assistant Secretary to the Medical Defence Union. The salary scale will range from £1750, rising by annual increments of £50 to £2000 p.a., and the successful applicant will be placed at a point on that scale according to his experience and qualifications for the appointment. The practitioner selected will be required to submit to a medical examination, and to contribute to the Union's superannuation fund.

Applications (12 copies), stating age, qualifications and medical experience, together with the names of 3 persons to whom reference can be made for further information, should reach the Secretary, The Medical Defence Union, Tavistock House South, Tavistock-square, W.C.1, not later than 30th September, 1958.

A large Pharmaceutical Company has a vacancy in the Medical Department for a Medical Practitioner (Male). A higher medical qualification would be an advantage but is not essential. The suitable applicant would be required to carry out those duties normally associated with this type of appointment including initiating and progressing clinical investigations. The work involves a certain amount of travel both in the United Kingdom and abroad. The Company operates a non-contributory Pension Scheme. Starting salary £1750.

Write, giving full details, to Address No. 411, THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2.

IMPERIAL CHEMICAL INDUSTRIES LIMITED
WILTON WORKS
invites applications for the post of full-time
ASSISTANT MEDICAL OFFICER

The successful applicant will be responsible to the Senior Medical Officer and will undertake the normal duties of an industrial medical officer. He will work in a large, recently opened medical centre which contains the latest equipment for basic and ancillary services.

Salary will be commensurate with age and experience, but not less than the B.M.A. minimum rate.

Experience in any of the following: general practice, casualty work, the Services; Industrial Medicine and or D.P.H., D.I.H., or other postgraduate qualifications would be an advantage.

An application form, together with further particulars, may be obtained from the Staff Manager, Imperial Chemical Industries Limited, Wilton Works, Middlesbrough, Yorkshire, quoting reference No. 515/113.

BRITISH GUIANA SUGAR PRODUCERS' ASSOCIATION have 2 vacancies for MEDICAL OFFICERS on their sugar estates starting 1st October.

(1) A temporary appointment on a single two-year contract.

(2) A permanent appointment, including a good contributory pension scheme, with 3-year tours of service in British Guiana.

Free living quarters, with basic furniture. Car allowance. U.K leave at the rate of 1 month for every year served overseas. Passages paid both ways for doctor, wife and children under 16. Minimum starting salary £1500.

Apply, in writing only, giving full details of qualifications and experience, and stating which post is applied for, to: The Medical Officer, Booker Brothers McConnell & Co. Ltd., Bucklersbury House, 83, Cannon-street, London, E.C.4.

M.R.C.P. London, 10 years Consultant Health Services, wishing to change job, seeks interesting post in industry. Would consider living Switzerland or Riviera. Good middle-handicap golfer. Fair tennis player.—Address, No. 412, THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2.

Group Sister. The United Kingdom Atomic Energy Authority, Industrial Group, requires a Sister in its Health and Safety Department at Windscale Works, Sellafield, Calderbridge, Cumberland, to act as deputy to the Senior Sister, and to assist with the organisation and operation of the works nursing service, which includes medical examinations and treatment facilities. The Medical Centre is under the general supervision of a Senior Medical Officer. Applicants must be State Registered Nurses. Familiarity with casualty and outpatient work is essential and experience of industrial health nursing is desirable. Salary will be assessed within the scale £605–£755, plus £30 p.a. for possession of the Occupational Health Nursing certificate. Contributory pension scheme, but the successful candidate may, if eligible, contribute to the F.S.S.N. Hostel accommodation may be available.

Send postcard for application form, quoting reference 2480, to Works Secretary United Kingdom Atomic Energy Authority, Industrial Group, Windscale Works, Sellafield, Calderbridge, Cumberland. Closing date: 28th July, 1958.

Doctors requiring applications, theses copied: Write to MANTON (WESTMINSTER) LTD., 98, Victoria-street, S.W.1 (VIC. 0141), who are specialists.

Part-time Consulting Rooms to be Let in Harley-street. Rents from £50 per half-day session. Apply: ELLIOTT, SON AND BOYTON, 86/87, Wimpole-street, London, W.1. WEL. 8367.

"Pregnancy Diagnosis by the Xenopus Method," 24-hour service. Send specimens of urine and £2 2s. fee. Hæmatology, Biochemistry, Flame Photometry.—WELBECK BIOLOGICAL LABORATORIES, 26, Park-crescent, Portland-place, W.1 (MUSeum 5386-7).

Microscopes. Highest prices paid for good modern types. Send or bring your equipment for valuation.—WALLACE HEATON LTD., 127, New Bond-street, W.1.

PUBLISHED by the PROPRIETORS, THE LANCET LIMITED, 7, Adam Street, Adelphi, in the County of London.
Printed by HAZELL, WATSON AND VINEY, LTD., Leigh Road, Slough and Aylesbury—Saturday, July 12, 1958.
PRINTED IN GREAT BRITAIN—Entered as Second Class at the New York, U.S.A., Office.

ENTIRELY NEW APPROACH

CHRONIC

RHEUMATIC DISEASES

INVOLVE BOTH

MUSCLES AND JOINTS

CODELPRONE

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(Multiple Compressed Tablets, Buffered Prednisolone with Meprobamate)

relieves BOTH joint inflammation and muscle spasm

'Codelprone' gives rapid relief from joint pain and stiffness, shortens the period of disability, and may reduce the incidence of permanent crippling deformity. Since 'Codelprone' contains both prednisolone and meprobamate it represents an **entirely new approach** to the treatment of chronic inflammatory diseases of muscle, tendons and joints.

Some Indications:

Rheumatoid arthritis, ankylosing spondylitis, osteoarthritis, synovitis, tenosynovitis, acute and chronic fibrositis, and certain allergic diseases where a prolonged, low dose of a steroid is required.

Composition

Each multiple compressed tablet contains: prednisolone 2 mg., meprobamate 200 mg., dried aluminium hydroxide gel 200 mg.

The basic N.H.S. cost of 21 tablets (average week's maintenance therapy) is 15/2d.

Literature gladly supplied on request.

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NOW — a favourite prescription

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more convenient for both patient and doctor

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Bellergal Retard

1 tablet night and morning

for **continuous** control

of symptoms in a wide variety

of psychosomatic disorders

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0.2 mg. total alkaloids of belladonna

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